INCIDENCE AND RISK FACTORS FOR ACUTE KIDNEY INJURY (AKI) IN PATIENTS UNDERGOING ISOLATED CORONARY ARTERY BYPASS GRAFTING (CABG) SURGERY.

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF M.Ch DEGREE (CARDIOTHORACIC SURGERY) EXAMINATION OF THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY, CHENNAI TO BE HELD IN AUGUST 2014.

CERTIFICATE

This is to certify that the thesis entitled "**INCIDENCE AND RISK FACTORS FOR ACUTE KIDNEY INJURY (AKI) IN PATIENTS UNDERGOING ISOLATED CORONARY ARTERY BYPASS GRAFTING (CABG) SURGERY**" is a bonafide work done by Dr. CHENGALATH MANORAS MATHEW, Christian Medical College Vellore, Tamilnadu in partial fulfilment of the rules and regulations for award of M.Ch Degree (Cardiothoracic surgery) under my guidance and supervision during the academic year 2011-2014.

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INTRODUCTION

13**Coronary artery bypass grafting (CABG) is** probably **the most common** adult **cardiac surgery performed**

world over. It is a myocardial revascularization procedure used in patients having coronary artery disease (CAD). With the rise in Ischemic Heart Disease in Indian population the incidences of Coronary Artery Bypass Grafting has drastically increased. Though percutaneous interventions are on the rise CABG remains the most durable means of revascularization for coronary artery disease. It prolongs life and provides more symptomatic relief(1). New onset

2**acute renal failure after Coronary** artery bypass **grafting**

(CABG) is a serious complication. This can lead to significant morbidity as well as mortality. CABG is a common surgery performed at our centre. The operation includes using a cardiopulmonary bypass machine and arresting the heart using cardioplegic solution. There are lots of vital parameter changes during and after the procedure which can lead to renal dysfunction. Though an uncommon complication after cardiac surgery, renal failure after CABG can be potentially fatal. The incidence of Acute Kidney Injury (AKI) depends on the type of cardiac surgery. The incidence is lowest after CABG, whereas it is high after valve or combined surgeries(2). This is the reason we planned to study only isolated CABG cases. There are reports studying the risk factors causing renal injury after coronary revascularisation (3–8), but there are hardly any studies on Indian population. Christian Medical College and Hospital is a tertiary care hospital in South India. We endeavoured to study those patients undergoing CABG, who are having normal preoperative renal parameters. We would like to find out the incidence of acute kidney injury among these patients in our institute. In addition we will also study the risk factors leading to renal dysfunction. This will help in the long run to prevent renal dysfunction in such patients. AIIMS AND OBJECTIVES To study the incidence and risk factors for AKI (Acute Kidney Injury) in patients with normal preoperative renal functions undergoing CABG in CMC hospital, Vellore. INCLUSION CRIETRIA: ? Patients undergoing exclusively CABG surgery in CMC Hospital. ? Patients with normal renal function prior to surgery as measured by serum creatinine. EXCLUSION CRITERIA: ? Patients with preop renal dysfunction and having high Serum Creatinine levels. ? Redo CABG ? Patients who underwent CABG along with other cardiac procedures. ? Off pump CABG (beating heart). MATERIALS AND METHODS Records of patients who underwent CABG between May 2013 and November 2013 were retrieved from the clinical database. From this group, all patients who had normal renal function as denoted by the preoperative creatinine and Glomerular filtration rates (GFR) were selected and their records studied. Details of 164 patients were collected retrospectively from the preoperative history sheet, clinical workstation and the intraoperative perfusion data sheet. Data would include the Demographics (age, sex) Other important medical illness Any medications Kidney function prior to surgery Details of surgery (Extent or severity of disease, Number of grafts done, duration of surgery, Bypass time, ischemic period) Intra-operative measurements (mean perfusion pressure, blood usage) Post-operative laboratory values. RIFLE criteria for acute kidney injury

used for the end point. This study was approved by the IRB (Institutional Review Board) of our institute. SURGICAL PROCEDURE: OPERATIVE STEPS: The chest was opened by a median sternotomy, the thymus was divided and the pericardium opened. The

13**left anterior descending artery** inspected and **the left internal mammary artery**

was harvested in all possible cases. Simultaneously the great saphenous vein was harvested. Systemic heparinisation was done to bring the ACT to 480 sec, aortic and single two stage venous cannulation were done and cardiopulmonary bypass was established. Marking of target vessels were done.

21**The Aorta was cross clamped and the heart was arrested** using **cold blood cardioplegia.**

Distal coronary anastomoses were performed using 8/0 prolene suture. Rewarming started at the completion of the last anastomosis. The cross clamp was released with root on suction. Next the proximal anastomoses were done using 6/0 prolene with side biting clamp. After coming off bypass, cannulae were removed in stages. Haemostasis was achieved. Pacing wires were taken if indicated. Drains - Pericardial and mediastinal were inserted. Left pleural drain was inserted when left internal mammary artery was harvested. Sternum was closed with stainless steel wires followed by standard wound closure. The patient was transferred with endotracheal tube in situ to the ICU. PERFUSION STATEGY: All surgeries were done on pump with the heart arrested. The perfusion apparatus consisted of a custom pack of Medtronic (Affinity) or Spictra (Capiox). Nonpulsatile perfusion was used for all patients. The flow rates used for most patients were 2.2 -2.4 litres/min/m2. Priming was done with crystalloid solution (Ringer Lactate). ANTIBIOTICS: All patients were given prophylactic antibiotics of Inj. Cefuroxime 25 mg/kg and Inj. Amikacin 10 mg/kg at the time of induction and followed by Inj. Cefuroxime twice daily and Amikacin once daily for 3 days. In patients with renal dysfunction, we use Inj. Ceftazidime 25 mg/kg and Inj. Augmentin 25 mg/kg at the time of induction and thrice daily for 3 days. In patients who develop renal dysfunction after surgery, the antibiotics are changed to Injectable Ceftazidime and Injectable Augmentin. In patients where severe infection is suspected blood cultures were taken and patients empirically started on Injectable Meropenem. When renal dysfunction was present in the post operative period, Meropenem was given in renal adjusted doses according to creatinine clearance. POST OPERATIVE MANAGEMENT:

19**In the Intensive Care Unit (ICU) patients**

were ventilated in SIMV (synchronous intermittent mandatory ventilation) mode. The tidal volume was set at approximately 8 to 10 ml/kg. The investigations (Haemoglobin, electrolytes, cardiac enzymes, arterial blood gases, an electrocardiogram and chest Xray) are sent. Neurological status is checked when the patient is fully awake. Sedation with either continuous morphine infusion or intermittent boluses was given. Inotropic supports were adjusted according to the hemodynamic status of the patient. Routine evaluation of serum potassium and ABG (arterial blood gases) were done in ICU. Investigations including blood urea and serum creatinine was sent everyday for 2 days. Patients were extubated next day morning if they were hemodynamicaly stable with no complications. The supports are tapered off on the second post operative day. All invasive lines are removed by day 3 of surgery. If satisfied patient is transferred to ward. A chest X

ray and electrocardiogram were done on the fifth postoperative day. They were discharged on the seventh or eighth postoperative day if the recovery was uneventful. RECORD COLLECTION Data was collected from various sources. History details were collected from the history sheet of the patient. Intra operative details were collected from the perfusion data sheet maintained in the theatre. Investigation details including all laboratory values were taken from the clinical work station on the intranet. After collection of creatinine values GFR (glomerular filtration rates) were calculated from the GFR calculator available at our CMC (Christian medical college) intranet. The Abbreviated MDRD (Modification of Diet in Renal Disease) was used for the same. These data were entered in the Epidata software for data evaluation. With the help of the statistician these data were evaluated. REVIEW OF LITERATURE Coronary artery disease (CAD) is caused by obstruction to the coronary arteries. It is usually due to atherosclerotic plaque in the coronaries. Due to this plaque the internal lumen is narrowed progressively resulting in reduced myocardial blood supply. Patients may get symptoms when this blood supply is reduced. HISTORY OF BYPASS GRAFTING: 1935 - Claude Beck reported placement of a pedicled pectoralis muscle flap on the abraded pericardium. (9) 1951 - Vineberg and Miller directly implanted the Internal Thoracic Artery (ITA) into the myocardium(Montreal)(10). 1953- Gibbon developed the cardiopulmonary bypass machine and thus the feasibility of direct coronary revascularization became possible.(11) 1954 - Murray considered direct anastomosis of Internal mammary artery to the coronaries (12). 1957 – Bailey did the first successful coronary endarterectomy(13) 1958 - Longmire reported a mammary-to coronary anastomosis. Perhaps this was the first IMA to coronary anastomosis. But actually it was performed after a surgical misadventure with a coronary endarterectomy.(14) 1962- Sabiston first reported use of a saphenous vein aorto-coronary bypass(15) 1957 - Sones & Shirey developed the coronary angiography at the Cleveland Clinic. This was considered paramount in planning an elective revascularization surgery (16). 1964 – Kolessov (Russian) is credited with the first successful planned sutured internal mammary-to-coronary anastomosis in 1964 (17) 1968 - Sen described myocardial acupuncture (18). 1971 - Effler began to revascularize using reversed saphenous vein grafts along with Favaloro based on the angiogram findings (19) Flemma, Johnson&Lepley described advantages of sequential grafting(20) 1970 -1985 - Various randomised studies were done to compare CABG and percutaneous interventions. The

> 8**three major trials, the Coronary Artery Surgery Study (CASS)(** 21), **the Veterans Administration** Coronary Artery Bypass **Cooperative Study Group(** 22) **and the European Coronary Surgery Study (ECSS)(**

23) demonstrate

> 8**the greatest survival benefit of revascularization.**

ROLE OF ATHEROSCLEROSIS IN DEVELOPEMENT OF CAD Fibrous plaque is formed from focal intimal lipid foci which gradually fill in the lumen to produce coronary stenosis. Complications like haemorrhage within the plaque, platelet aggregation and thrombosis cause acute MI or unstable angina. When myocardial blood flow is sufficiently impaired in relation to myocardial oxygen demands, myocardial necrosis occurs. This may lead to subendocardial ischemia or transmural necrosis. Atherosclerosis usually involves the proximal portion of major coronary arteries and the first of the secondary branches. If reperfusion occurs within 3 to 4 hours of MI, infarct size as well as mortality is reduced. Healing of the acute myocardial ischemia leaves a scarred area of myocardium. When the scar area is almost all fibrous tissue,

it is usually large and the left ventricular wall may become akinetic or anneurysmal. Repeated ischemic events may occur jeopardising function of heart. DIAGNOSIS OF A PATIENT WITH CAD Symptoms suggestive of angina pectoris or acute MI can help think towards CAD. ECG perhaps is the most common everyday practical test done to diagnose ischemia. Echocardiography (ECHO) will show regional wall motion abnormalities and identify left ventricular dysfunction. Angiography is the definitive and gold standard diagnostic procedure (16). PRESENTATION STABLE ANGINA: Chest discomfort or pain during exercise or stress occurs because of disproportionate blood supply to the myocardial demand and reduced coronary reserve resulting from coronary atherosclerosis. UNSTABLE ANGINA: Severe and persisting angina with ECG changes and only minor enzymatic elevation. It is an ominous symptom. It is caused by unstable atheromatous plaque, which fissures or ruptures and sometimes a thrombus overlies. ACUTE MI (Myocardial Infarction): It is because of partial of complete occlusion of a coronary artery wherin the collateral blood supply is not adequate. It mostly occurs with unstable atheromatous plaques. Some patients may have repeated coronary events when the plaques are unstable. Severe proximal Left Anterior Descending artery (LAD) lesions have acute and fatal MIs. Sudden cardiac death can result from severe myocardial ischemia resulting in ventricular fibrillation, asystole or severe LV dysfunction. Overall survival in a medically treated heterogeneous group of CAD is 75% at 5 years, 60% at 10 years and 45% at 15 years (24). WHEN IS CABG INDICATED:(25): Asymptomatic or Mild Angina: Class I 1. Ischemia with no symptoms/

> 11**mild angina with** major **left main disease.** 2. Ischemia **with**

no symptoms/

> 11**mild angina with left main** Equivalent **disease.** 3. Ischemia **with**

no symptoms/ mild angina with triple vessel disease. 4. No symptoms/ mild angina with disease in proximal part of LAD. 5. No symptoms/ mild angina with

> 5**single or double vessel disease,** but without **involvement of** proximal **LAD.**

Class IIa 1. No symptoms/ mild angina with disease in proximal LAD, with single or double vessel disease. Class IIb 1. No symptoms/ mild angina with single or double vessel disease. These patients have no disease in proximal LAD. Patient having stable angina Class I 1. Stable angina with left main disease. 2. Stable

> 11**angina with left main** equivalent **disease.** 3. Stable **angina with triple vessel disease.**

4. Stable angina with double vessel disease with disease in proximal LAD. These also have an ejection fraction < 50% and positive noninvasive testing. 5. Stable angina with

5single or double vessel disease with a greater area of

viable myocardium. 6. Stable angina with intolerable angina even with maximal medical management. Class IIa 1. Stable angina with disease in proximal LAD as only a single vessel disease. 2. Stable angina

5with single or double vessel disease and

no disease in proximal LAD. Class III 1. Stable angina

10with single or double vessel disease without

disease in proximal LAD. 2. Stable angina with no major coronary disease. These patients also had a negative noninvasive testing. 3. Stable angina with minor disease in coronaries. Unstable Angina/Non–ST-Segment Elevation

3MI Class I 1. Major disease in left main coronary artery. 2. Major left main equivalent

disease. 3. Unstable angina or non–ST-segment elevation MI in patients. These are patients without any benefit of medical management. Class IIa 1.

5Single or double vessel disease with disease in proximal LAD.

Class IIb

51. Single or double vessel disease without disease in

proximal LAD. These are patients where the conditions are not favourable for percutaneous procedures.. ST-Segment Elevation MI (STEMI) Class I 1. Need for an urgent CABG a. Failed angioplasty and having ongoing pain b. Ongoing pain with no response to medical management. These patient are not candidates for PCI c. complications of septal ruture or mitral valve insufficiency d. Cardiogenic shock e. Life-threatening ventricular arrhythmias Class IIa 1. Failed PCI with suitable anatomy and early presentation. Class III 1. Persistent angina with only a small area of myocardium at risk.

3Poor LV Function Class I 1. Major left main coronary artery stenosis. 2. Left main equivalent

disease. 3. Triple

10**vessel disease involving proximal LAD. Class**

IIa 1. Major viable revascularizable myocardium. Class III 1. Without significant revascularizable viable myocardium.

3**Life-Threatening Ventricular Arrhythmias Class I 1.** Caused by **left main coronary artery stenosis. 2.** Caused by triple **vessel disease.**

3. Post resuscitation from sudden cardiac death or sustained ventricular tachycardia Class IIa 1. Bypassable single

10**or double vessel disease.** 2. Disease in **proximal LAD.**

Class III 1.

3**No evidence of ischemia. CABG after failed PTCA Class I 1.**

Doubt of a greater area of myocardium being jeopardised with continuing ischemia. 2. Hemodynamically unstable. Class IIa 1. for removal of a foreign body. 2. hemodynamically unstable with coagulation abnormalities. Class III 1. No ischemia. 2. Not able to do a satisfactory revascularisation. Patients with previous CABG Class I 1. Intolerable chest pain even with maximum medical management. 2. No flow in previous done grafts and having class I indications. PREOPERATIVE MEDICATIONS Patients can continue beta blockers, calcium channel blocker and ACE inhibitors till the operation. There are evidence to support that preoperative beta blockers usage has decreased the postoperative atrial fibrillation(AF) (26). Digitalis can be used intraoperatively or postoperatively for rate control if there is AF. Antiplatelet agents are usually stopped 1 week prior to the surgery. SURGERY: The main aim of any revascularization surgery is to bypass all major and branch vessels of 1 mm or more diameter with severe stenoses (50% diameter reduction) (27). Sequential grafting may be required because of scarcity of grafts. To increase the patency of such grafting, the distal end to side anastomosis has to be done to a large vessel with tight proximal stenosis and good distal run off. The commonly used graft strategy is

14**anastomosis of** left **internal mammary artery** (LITA) **to left anterior descending artery (LAD).**

Other coronaries are grafted with saphenous vein. Radial artery grafts are used for good targets with proximal stenosis 70% or more. Coronary angiogram provides the key information to plan CABG but on table observations will also help to decide about grafting the vessels. WHAT ARE THE VARIOUS CONDUITS FOR REVASCULARISATION? VENOUS GRAFTS Venous grafts are commonly taken from the legs; usually the great saphenous vein is used. Most centres over the world use saphenous vein in most of the patents. Therefore in reoperations alternate conduits like the short saphenous vein, right internal

thoracic artery, radial artery, right gastroepiploic and in rare cases cephalic vein , splenic artery and ulnar arteries may be used. Varicose veins are unsuitable as graft conduits, whereas superficial varicosities are not. TECHNIQUE OF HARVESTING SAPHENOUS VEIN: The legs are abducted and knees are flexed about 45º. Incision is made anterior to medial malleolus to harvest lower segment, whereas groin incision is made for upper segments and extended according to the length needed. Care is taken not to create flaps while harvesting the vein so as to prevent skin necrosis. The saphenous nerveis also preserved. External diameter of 3 to 3.5 mm is considered satisfactory. A single long segment of great saphenous vein of about 50 to 65cm is harvested. Usual requirement for diagonal graft is 12 to 15 cm of vein length, wheras for marginal grafts (20 to 24 cm) and right coronary artery and its branch grafts (18 to 22 cm) will be needed. The branches are ligated or clipped just flush with the vein wall to avoid diverticula or luminal narrowing. The subcutaneous tissue and skin are sutured subsequently. To harvest the short saphenous vein, patient is placed in prone position and incision is started posterior to the lateral malleolus. Here the sural nerve is preserved which runs parallel to it. After dividing the vein subcutaneous tissue and skin are sutured. Endoscopic vein harvesting can also be done. This reduces pain and wound complications, but is more time consuming than the conventional method. The harvested vein is distended with solution, the leaking branches looked for and are clipped or ligated. It is advisable to preserve this harvested venous graft in balanced salt solution to prevent endothelial damage till we anastomose it (28). ARTERIAL GRAFTS:

18**Internal Mammary Artery (Internal Thoracic Artery)(**

IMA/ITA): Usually the left IMA is harvested as a choice of graft to the Left Anterior Descending Coronary Artery. It is mobilised after sternotomy. There are standard sternal retractors which help to elevate left sternal edge and thus the left internal thoracic artery is exposed. It can be harvested as skeletonised or pedicled graft. Incision is made medial to the IMA using low power electrocautery and extended along the whole length. The pleura may be widely opened to get better exposure. Nevertheless extrapleural harvesting can also be done. The phrenic nerve is to be carefully dealt with and preserved at the proximal end. With slight traction, intercostal braches can be identified, clipped and divided. After heparinisation, the distal end is divided. The IMA is checked for good flow. It is wrapped in gauze soaked with papavarine solution till heart is taken on bypass. Once the distal anastomosis with the vein grafts are finished, the IMA is anastomosed to LAD using 7-0 or 8-0 polypropylene suture. The IMA can be sequentially grafted to diagonals and LAD. Skeletonization preserves the sternal blood supply. Thus it is preferable in conditions where the risk of infection is high like obesity, diabetes and bilateral internal thoracic artery harvesting. Radial Artery: The prerequisite for using the radial artery is that the palmar arch should be intact. The best way of making it sure is the by doing the Allen's test. It is performed in the non dominant hand before surgery to make sure that palmar arch gets supply from the ulnar artery after removing the radial artery. The patient is asked to clinch his fist for 30 seconds. The radial and ulnar arteries are occluded with fingers. The hand is opened now and the palm will be seen to be blanched. On releasing the occlusion on the ulnar artery, the palm should become flushed within 5 to 6 seconds. This denotes adequate blood supply to the palmar arch by the ulnar artery and a negative Allen's test. The arm is positioned by the side. A separate draping is done. Incision is made over the radial pulse in the wrist and extended proximally. Dissection is done and the branches are clipped and divided. The artery is removed after ligating both ends. The artery is irrigated and dilated with ringer lactate solution containing heparinised blood and sodium nitroprusside. Radial artery is known to undergo spasm. The irrigation is done to prevent this spasm. The artery is immersed in the same solution until it is anastomosed. Right Gastroepiploic Artery (GEA): The Midline sternotomy incision is extended upto the point midway between xiphisternum and

umbilicus. The abdomen is entered and the liver is retracted to the right side. Right GEA branches are ligated and divided along the greater curvature for required length. The pedicle is passed either anterior or posterior to the duodenum, then through a diaphragmatic opening made medial to the inferior venacava opening. Though this graft can be used to bypass most of the coronary arteries, it is commonly used to graft the distal RCA or Posterior Descending Artery (PDA). Inferior Epigastric Artery (IEA): It is harvested through a paramedian incision. It originates from external iliac artery along the medial edge of deep inguinal ring. It then ascends obliquely toward the umbilicus. It has a mean length of 13 cm and a mean diameter of 2.4 mm. The artery is wrapped in gauze soaked in papaverine and immersed in the same solution until it is used. Splenic Artery: It is used rarely when other conduits are not available. Midline sternotomy is extended down to a point midway between xiphisternum and umbilicus. The lesser sac is opened. The splenic artery branches to pancreas are ligated and divided. The artery is divided at the hilum. Splenectomy is not needed as it is supplied by short gastric branches of left gastric artery also. The splenic artery is passed through a diaphragmatic opening made medial to the inferior vene cava and anastomosed to branches of RCA and LCX. DISTAL ANASTOMOSES: The epicardium over the selected coronary vessel is marked. Clearing of the anterior surface of the artery is done gently with the help of scalpel. The anterior wall of the artery is opened with sharp blade slightly obliquely to prevent opening of posterior wall. Arteriotomy is extended on both sides to a length of 4 to 6 mm. The end of the venous conduit is bevelled and incision is made to make opening 10 to 20% larger than the arteriotomy. The sutures are placed little away from the margin in the vein. The coronary artery suture pierces the intima near the edge and comes out several millimetres away from edge. The stitches are placed separately. The double armed sutures are started at one corner of the arteriotomy and continued either clockwise or anticlockwise to tie with the other arm of the suture. For sequential anastomoses, if the vein is of adequate size, it can be opened perpendicular to the long axis. The incision should not exceed one third of the circumference. The anastomosis is begun in the middle of the venous opening and continued around and tied. If the vein is small or if radial artery or ITA is used, it is opened parallel to its long axis. The diamond anastomosis is made. After each anatomosis, the conduit is distended to avoid excess length or tension between sequential anastomosis. PROXIMAL ANASTOMOSES: After releasing the aortic cross clamp, a partially occluding side biting clamp is applied on the ascending aorta. Hole is made in the aorta using aortic punch. Conduits are positioned in such a way that they are not kinked or tense. The proximal end is cut obliquely and incised to create a circumference 10 to 20% larger than aortic opening to form cobra head at the completion of anastomosis. A double armed 6-0 polypropylene suture is used for the anastomosis. If the aorta is severely calcified, proximal anastomosis can be done without side biting clamp, while the heart is still arrested.

3**During off pump coronary artery bypass surgery,** proximal anastomosis **is**

done before distal anastomosis. MANAGEMENT IN THE POSTOPERATIVE PERIOD EARLY: It is advised to start Aspirin 150 mg, as soon as the chest drainage settles, preferably within first 6 hours of surgery and continued once daily thereafter to enhance the vein graft patency(29). Oral beta blocker is given 4 to 6 hours postoperatively. This is balanced against ionotrope use in the ICU. Ideally it is continued as a prophylaxis against supraventricular arrhythmias (30). Digitalis is not routinely used because it may produce atrial and ventricular arrhythmias. The patients may develop 10 to 20 % fall in blood pressure 8 to 12 hours after surgery with good pedal pulses and cardiac index >2. Some patients may require low dose dopamine (3.5 mics/kg/min).

14**Intra Aortic Balloon Pump is** occasionally required **for patients who have**

low cardiac output with high left atrial pressure or presence of intractable ventricular arrhythmias intraoperatively or in the immediate postoperative period. LATE: CABG is only a palliative procedure. It only ensures revascularisation. But it is par essential to educate patients about their condition so as we as clinicians ensure the graft is patent for a long time. The most powerful predictor of survival is the use of LIMA TO LAD. Aspirin should be administered immediately after surgery and continued for at least 1 year postoperatively is the well established effective regimen (31). Control of atherosclerosis risk factors retards and even reverse atherosclerosis in the vein grafts. Smoking must be stopped. Body weight should be maintained, special dieting is followed if required. Hypertension and saturated fat in diet must be controlled. Serum lipids must be maintained within normal limits either with diet or drugs (32,33). SURVIVAL: The survival rates after isolated CABG are 98% at 1 month, 97% at 1 year, 92% at 5 year, 81% at 10 year and 66% at 15 year or more (34) MORBIDITY: NEUROLOGICAL: Postoperative neurological deficit is the important cause for morbidity and mortality. The incidence may be approximately 5 to 6%. There are two types(35). Type I deficit –

10**major focal deficits, stupor, and coma.**

It accounts for 3.1%. The predictors are aortic atherosclerosis, previous

3**history of neurological disease, use of intra aortic balloon pump** (IABP), **diabetes.**

Type 2 deficit – deficit in intellectual and memory. It accounts for 3%. MEDIASTINITIS: It is one of the devastating complications to occur. Deep sternal wound infection seen in < 5% of patients who undergo CABG with CPB and increases the mortality (36). Obesity is a risk factor. Other risk factors are diabetes mellitus, previous CABG and use of both IMAs. RENAL DYSFUNCTION: This topic is taken up separately at the end of review of literature. Renal dysfunction increases the mortality from 0.9% (without renal impairment) to 1.9% (with renal impairment). The preoperative risk factors are advanced age, moderate to severe cardiac failure, previous CABG, diabetes mellitus & previous renal disease. This complication was similar in both CABG groups with and without CPB in many studies. INCREMENTAL RISK FACTORS FOR DEATH: Most deaths after CABG are from cadiac failure. About 25% of deaths are not related to coronary artery disease or the operation(37). It is paramount to understand these factors. PATIENT SPECIFIC: AGE : Older age is a risk factor for prolonged hospital stay and early complications. SYMPTOMS OF ISCHEMIA : Canadian angina class and unstable angina grade, higher the grade the risk is increased. NONCARDIAC COMORBIDITY: Various noncardiac factors may play in increasing the morbidity. Obesity, hypertension, diabetes mellitus, hypertriglyceridemia, history of smoking, low FEV1 %, history of peripheral vascular disease, or a history of surgery for the same, history of cerebrovascular disease and renal failure are all risk factors for early death after CABG (38). CARDIAC COMORBIDITY: Associated cardiac conditions such as mitral regurgitation, aortic regurgitation, atrial fibrillation, ventricular arrythmias and requirement of a cardiac pacemaker increase the postoperative morbidity and mortality. LEFT VENTRICULAR FUNCTION: Patients who presents with cardiogenic shock after myocardial infarction, higher NYHA class limiting the activity and low ejection fraction will adversely affect the outcome after surgery. The presence of low

ejection fraction associated with mitral regurgitation increases the risk above that of low ejection fraction alone. CONCOMITANT PROCEDURES: Left ventricular reconstructive procedures will increase the mortality rate. QUALITY OF LIFE: Most of the patients get a good quality of life. This good quality gradually declines 5 years post surgery. The use of arterial line filters has reduced the incidence of neurobehavioral and cognitive dysfunction. Prevalence is affected by pre and post operative anxiety, depression and old age. Gross deficits result from embolisation of ascending aortic atherosclerotic debris, air or intracardiac thrombus rather than CPB effects.

18**Prevalence is** roughly **0.5% in young,, but** raises **to** 5% **in**

older people and about 8% in patients over 75 years(38). Almost all studies show a decrease in the use of beta blocker and vasodilator medications after CABG. Maximal exercise capacity is also improved by CABG and ECG abnormalities are importantly reduced. GRAFT PATENCY: INTERNAL THORACIC ARTERY: IMA is an excellent conduit for CABG. About 90% of the left IMAs anastomosed to LAD are patent at 10 to 20 years after operation and closure after that is uncommon. However 5 to 10% of grafts have stenoses late postoperatively, most of which do not progress to occlusion. Various factors favour the excellent performance of IMA. It is partially because of continued functioning of endothelial cells, which secretes endothelial derived relaxing factor and prostacyclin. It has inherent property to resist development of atherosclerosis. Another important factor in grafting to LAD is the large runoff through the diagonal and septal branches. It has been seen that use of bilateral ITAs increases survival. But wound complications are more common particularly in obese and diabetic patients when bilateral IMA is harvested. RADIAL ARTERY: Early patency of radial artery exceeds 90%. Native coronary artery stenosis of less than 70% reduces the patency rate (39). GASTROEPIPLOIC ARTERY: Its early patency rate within one year is 94%, between 1 and 5 years is 88% and between 5 and 10 years is 83% (40). INFERIOR EPIGASTRIC ARTERY: Early patency was 98% and late patency was 93%. Graft patency is improved when anastomosed to a vessel with proximal occlusion of 60% or more(41). SAPHENOUS VEIN GRAFT: Intimal hyperplasia is found universally in venous grafts after 1 month of surgery. This process is not progressive. Thickness of the hyperplasia is inversely proportional to the flow rate, so it is considered as a remodelling process. Atherosclerotic lesions may not be found in grafts of less than 3 ½ years duration. By 10 years, most of the grafts have some atherosclerotic changes sometimes severe in nature. Whether these changes result from morphological damage during harvest and insertion or by patient's tendency or by both is uncertain. Hyperlipidemia is a risk factor for extensive vein graft atherosclerosis. Thrombosis of venous grafts can reduce the patency early postoperatively which results from endothelial loss and exposure of basement membrane to blood. It can also develop late in heavily atherosclerosed areas. Because of these reasons 10% of graft closure occurs within few postoperative weeks, particularly when antiplatelets are not used. Lesser saphenous vein patency rate appears to be equal to the great saphenous vein. Upper limb veins have lower patency rates. When there is unavailability of these veins, cryopreserved allograft veins can be used, which have very low late patency rates. CABG AND RENAL FAILURE

19**Acute kidney injury (AKI)** is **loss of** kidney **function**

precipitously. Urea is accumulated and so are the nitrogenous compounds. Initially well known as acute renal failure (ARF) now the term AKI is used. ARF term should be used for severe AKI, usually when a form of renal replacement is required.(42) Several definitions of AKI have been developed in order to provide a uniform definition of AKI. In 2004, the Acute Dialysis Quality Initiative (ADQI) group gave guidelines

management of AKI. When they felt the great need for a standard definition for AKI, they proposed

17**the RIFLE criteria** (43). **A modification of the RIFLE criteria was** later given **by Acute Kidney Injury Network**

(AKIN) (44) We have followed the RIFLE criteria in our study. RIFLE CRITERIA RIFLE gives 3

2**grades of increasing severity** for any form **of acute injury** to kidneys – **risk (class R), injury (class I) and failure (class F) – and two outcome classes (loss and end-stage kidney disease)(** 45). **A unique feature of the RIFLE classification is that it provides three grades of severity for acute kidney injury based on changes in either serum creatinine or urine output from the baseline condition. This allows classification** of patients **with acute kidney injury into one of the three RIFLE**

severity classes.

1**●Risk — 1.5-fold increase in the serum creatinine, or** glomerular filtration rate **(GFR) decrease by 25 percent, or urine output <0.5 mL/kg per hour for six hours ●Injury — Twofold increase in the serum creatinine, or GFR decrease by 50 percent, or urine output <0.5 mL/kg per hour for 12 hours ●Failure — Threefold increase in the serum creatinine, or GFR decrease by 75 percent, or urine output of <0.3 mL/kg per hour for 24 hours, or anuria for 12 hours ●Loss — Complete loss of kidney function (eg, need for renal replacement therapy) for more than four weeks ●ESRD — Complete loss of kidney function (eg, need for renal replacement therapy) for more than three months**

The change in serum creatinine was specified as occurring over not more than seven days. PATHOGENESIS OF AKI: The development of postoperative AKI is usually due to various preoperative, intraoperative and postoperative factors. The preoperative factors are usually patient related. The intraoperative factors mostly due the CPB and the surgery per se. (7,46,47). Kidneys are prone to ischemic damage. Renal arteries are endarteries. There are some effects of CPB that can cause renal injury. These alterations may be in the blood flow, low cardiac output, hemodilution, renal vasoconstriction, and loss of pulsatile flow during CPB (7,46,48). These factors causes an imbalance in oxygen supply/demand to the kidney causing cellular injury (49,50). There is a correlation between hypothermia during CPB and AKI (51,52). The causative mechanism seems to be related to the increased metabolic demand with the subsequent nephron damage

15**due to low perfusion temperatures as** the **result of hypoperfusion of the**

superficial cortex that occurs during rewarming **and restoration of normothermia**

(51). The CPB-induced systemic inflammatory response is an important cause of renal injury. It causes interstitial inflammation with tubular injury(53,54). During CPB the blood cells are exposed to nonphysiologic surfaces leading to cell lysis (55). These destroyed red blood cells release

7**plasma free hemoglobin into the circulation causing occlusion of renal tubules with hemoglobin casts and necrosis of tubular cells**

(55). Last but not the least CPB causes embolization of particulate matter (56). Studies have shown that emboli counts were independently associated with postoperative AKI (57). AKI is an accepted serious complication after coronary revascularisation. This increases morbidity and mortality. The stay in hospital is also increasesd(58). The risk of Acute Kidney Injury (AKI) varies from 3-30% (58,59). The mortality rates increases when AKI leads to requirement of dialysis.

4**MODIFICATION OF DIET IN RENAL DISEASE FORMULA(** 60) **The MDRD equation was developed in 1999.**

The Cockcroft-Gault formula estimates creatinine clearance. MDRD study estimates GFR by measuring 125I-iothalamate urinary clearance. The values were taken from patients with established CKD. There are many MDRD equations. The more commonly used one is the abbreviated (four-variable) MDRD equation. Age, sex, racial factor are all used.

4**Glomerular Filtration Rate (GFR) Equations ? Cockcroft-Gault formula = ([140 − age] × weight)/(72 × SCr)**

4**(Multiply by 0.85 if female; expressed in mL/min.)**

?

4**Abbreviated MDRD equation = 186 × (SCr−1.154) × (age−0.203)**

4**(Multiply by 0.742 if female, by 1.212 if African American; expressed in mL/min/1.73 m2)**

THE DEBATE ON TAKING A LOWER GFR VALUE AS NORMAL FOR INDIAN POPULATION: A normal

reference range for

> 9**glomerular filtration rate (GFR) in** adult Indian **potential kidney donors**

has not been determined. The values from a western population are being used as reference. On the whole population in India has a lower body surface area as compared to the west. Thus it is important to understand that the GFR values which fall in mild renal dysfunction may be normal for Indian population. The normal GFR for an Indian is considerably lower than western population(61). The mean GFR would be 81.4 ±

> 16**19.4 ml/min/1.73 m2** BSA, **which is** much lower than **the normal value of** 110–120 **ml/min** derived from **a western population.**

Various Indian studies take in the value of GFR of approximately 60ml/min/1.73m2 as normal for Indian population(62,63). We have also taken normal GFR as 60ml/min/1.73m2 for our study. RESULTS We studied 164 consecutive patients between May 2013 and November 2013. These 164 patients had a normal creatinine value prior to surgery. The normal creatinine value defined by our CMC biochemistry laboratory is 1.4mg/dl. Of these patients only 126 patients had a normal GFR. The normal GFR was taken as 60ml/min/1.73m2 for our Indian population(62,63). There were 126 patients that satisfied these criteria. We studied the risk factors for AKI in 3 parts – preoperative, intraoperative and postoperative factors. We studied factors in general population of patients as well as in two groups, i.e. one group which developed Acute Kidney Injury (AKI) and the other which did not develop AKI. A GFR reduction of >25% was taken as class R Acute Kidney Injury (rifle criteria). The Variable Mean Std. Dev. Min Max incidence of AKI in our study was 23.02%. The general demographics are as below: age 57.26 6.97 33 73 weight 63.27 9.85 38 89 Preop_creat 1.08 0.15 0.74 1.76 Preop_gfr 73.45 10.99 60.12 99.98 Tpt (Total pump time) 92.38 25.78 31 163 Ischemic time 48.30 12.73 19 83 mean perfussion pressure 53.22 5.68 40 73 Post pump hemoglobin 10.45 1.04 8.1 13.4 Variables Groups n % Sex male 113 89.68 female 13 10.32 Diabetes yes 68 53.97 no 58 46.03 Hypertension yes 86 68.25 no 40 31.75 Copd yes 1 0.79 no 125 99.21 Stroke yes 3 2.38 no 123 97.62 lvd yes 39 30.95 no 87 69.05 AKI N % YES 29 23.02% NO 97 76.98% 23% 77% AKI YES NO PREOPERATIVE FACTORS: AGE: The mean age in our study was 57 years with the youngest being 33 and oldest being 73. Most patients were between 51-60 years. The age distribution is shown below: age Freq. Percent 30-40 2 1.59 41-50 19 15.08 51-60 64 50.79 61-70 39 30.95 71-80 2 1.59 age groups 60 50.79 50 40 30.95 30 20 15.08 10 1.59 1.59 0 30-40 41-50 51-60 61-70 71-80 48.2% of those who had reduction were >60 years of age. Though a causal relationship could not be established, it seems AKI is more prone in older age. Variables Groups gfr_red No Yes Total p-value <=50 17 4 21 % 17.53% 13.79% 16.67% Age 51-60 % 53 54.64% 11 37.93% 64 50.79% 0.118 >=61 27 14 41 % 27.84% 48.28% 32.54% Total 97(76.98%) 29(23.02% 126(100%) SEX: Males were predominant in our study. There were 113(89.68%) males and 13(10.32%) females. Variables Groups N % % male 113 89.68 Sex male female female 13 10.32 10% 90% The following is the table which shows the average males and females in the two groups of AKI and non AKI: Variables Groups gfr_red No Yes Total p-value Male 88 25 113 Sex % Female 90.72% 9 86.21% 4 89.68% 13 0.483 %5 9.28% 13.79% 10.32% 86.2% (n=25) of AKI patients were men, but the total number of women in the study (n= 13) was too small to draw any conclusions. DIABETES AND HYPERTENSION: There were 68 patients with diabetes (DM) and 86 patients had hypertension (HT), while 54 patients had both. The incidence of AKI in patients with both DM and HT was

found to be higher. Variables Groups n % Total yes 68 53.97 Diabetes no 58 46.03 Total yes 86 68.25 Hypertensives no 40 31.75 Variables Groups gfr_red No Yes Total p-value no 21 21.65 5 17.24 26 20.63 ht_dm ht 25 25.77 7 24.14 32 25.4 0.676 dm 12 12.37 2 6.9 14 11.11 both 39 15 54 40.21 51.72 42.86 STROKE: Three patients had stroke prior to study. None of these patients developed AKI. LEFT VENTRICULAR DYSFUNCTION: 12 of 29 patients who developed AKI had left ventricular dysfunction. Variables Groups n % lvd yes 39 30.95 no 87 69.05 left ventricular dysfunction yes no 31% 69% Of the lvd group, there were only 2 patients with severe LVD (<30%), and roughly 72% of had moderate LVD (31-45%). Only 23% had mild LVD. AKI was seen more in moderate LVD group. No association was found in patients with severe LVD. Variables Groups gfr_red No Yes Total p-value <=30 2 7.41 0 0 2 5.13 LVD 31-45 19 70.37 9 75 28 71.79 0.625 >=46 6 22.22 3 25 9 23.08 PREOPERATIVE CREATININE VALUES: Preoperatively the mean creatinine of the study was 1.13 mg/dl PREOPERATIVE GFR VALUES: The mean preoperative GFR was 73 ml/min/1.73m2. The least and maximum values being 60 and 90ml/min/1.73m2 respectively. PREOPERATIVE HEMOGLOBIN AND LACTATE VALUES: The mean preoperative haemoglobin was 12gm/dl, whereas the mean lactate values were 1.29millimoles/L. INTRAOPERATIVE FACTORS: DURATION OF CARDIOPULMONARY BYPASS: The mean duration of Cardiopulmonary bypass (CPB) of the whole group was 92 minutes (range 31 – 163 minutes). Whereas the mean Ischemic time (the cross clamp time) was 48 minutes (range 19-83 minutes). The mean duration of CPB in AKI group was 94.9 minutes. This was greater than the group having no AKI. n mean sd min median max p-val No GFR reduction 97 91.64 25.3 31 94 163 GFR reduction 29 94.9 27.64 48 98 150 0.55 The mean duration of Ischemic time in AKI group was 51.93 minutes. There was no statistical significance between these groups. n mean sd min median max p-val No GFR reduction 97 53.61 5.76 40 54 73 GFR reduction 29 51.93 5.34 42 52 66 0.16 MEAN PERFUSION PRESSURE: (MEAN ARTERIAL PRESSURE): The entire group had a mean perfusion pressure of 53mmHg (range 40-73mmHg). Though 41% of those developing AKI were having a mean perfusion pressure of <50, a causal relationship could not be established statistically. 30% patients with perfusion Variables Groups gfr_red No Yes Total p-value <=50mmHg 28 12 40 % 70% 30% 100% MPP 50-60mmHg % 57 78.1% 16 21.9% 73 100% 0.238 >=61mmHg 12 1 13 % 92.4% 7.6% 100% (12/40) mean pressure(MPP) less than 50mmHg developed AKI, while only 7.6%(1/13) patients with MPP >61 had AKI. The incidence of AKI was 4 times more when the MPP less than 50mmHg. NUMBER OF GRAFTS: Most of patients who had renal dysfunction had 3 grafts (64%). Only 8(27%) of 29 patients who were grafted with 4 vessels developed AKI. Thus the number of grafts may not be a major factor in causing AKI. More number of grafts means more the duration of CPB. POST BYPASS HEMOGLOBIN: The mean post bypass haemoglobin was 8.0gm/dl (range: 5.6 – 10.5). . There were only 2 patients with post pump haemoglobin <8gm/dl and one (50%) developed AKI. There were 70 patients with post pump haemoglobin >8gm/dl and 12 (17.1%) of them developed AKI. post_phb GFR_red NO YES p-val <8 n 39 17 % 40.21 58.62 >=8 n 58 12 % 59.79 41.38 0.08 There was progressive increase in incidence of AKI as post pump haemoglobin decreases. There was no statistical significance found. POST BYPASS LACTATE: The average post bypass lactate was 3.35millimoles/L. 12 of 53 (22.6%) patients having lactate levels of <3millimoles/L developed AKI. 7 of 39 (17.9%) patients having lactate levels between 3-4millimoles/L developed AKI. 10 of 34 (29.4%) patients having lactate levels >4millimoles/L developed AKI. Groups GFR reduction No GFR redction total P value Post <= 3 41(77.4%) 12(22.6%) 53(100%) pump 3.1-4.0 32(82.1%) 7(17.9%) 39(100%) 0.508 lactate >=4 24(70.6%) 10(29.4%) 34(100%) Increased incidence (29.4%) AKI with post bypass lactate levels of >4 mmol/l was seen. BLOOD PRODUCTS: Blood (packed cells) was used in 78 patients(61.9%). 19(24%) of these patients developed AKI. The incidence of AKI increased as the number of units of blood transfused increased. Those transfused with more than 3 units of blood had more than three times the incidence of AKI compared to those only one unit A statistical was not achieved Variables Groups 0 gfr_red No 38 79.2% Yes 10 20.8% Total 48 100% p- value who had transfused. significance though. PRODUCTS WB 1 2 35 87.5% 16 66.7%

5 12.5% 8 33.3% 40 100% 24 100% 0.066 >=3 8 57.2% 6 42.8% 14 100% no GFR reduction GFR redction total Xaxis: units 48 of blood used 38 40 35 24 16 14 10 5 8 8 6 nill one two three ULTRAFILTRATION: Was done only in one patient. RETROGRADE AUTOLOGOUS PRIMING (RAP): Overall 30 (23%) patients underwent RAP. Variables Groups n % rap Yes No 30 96 23.81 76.19 20% of patients who underewent RAP developed AKI; wheras 33% of those who did not undergo RAP developed AKI. GFR reduction RAP NO YES p-val YES (TOTAL 30) 25 5(20%) NO (TOTAL 96) 72 24(33%) 0.344 POSTOPERATIVE FACTORS: REEXPLORATION: There was only one re-explorations done for increased postoperative drainage. DIALYSIS: none of the patients were dialysed in the postoperative period. HOPSITAL STAY: the mean duration of postoperative stay was 6 days. MORTALITY: Only one patient died of recurrent ventricular fibrillation. DISCUSSION: Definitions of renal dysfunction have been used varyingly in literature. Some have used absolute values of postoperative cut off creatinine values as 1.5mg/dl (64,65), as >2.1mg/dl (6), as doubling of baseline creatinine values (3,66) while some have used creatinine clearance of <50ml/min (67)as a marker. Various formulas of estimated Glomerular Filtration Rate (GFR) like Cockroft-Gault formula for Creatinine Clearance (5,68) and the

20**Modification of Diet in Renal Disease (MDRD) formula for Estimated Glomerular Filtration Rate**

(eGFR) has been used. Others have also defined AKI as only when a deterioration in renal function requires dialysis(69,70) We used the abbreviated MDRD formula for calculation of GFR. We also used the RIFLE criteria (45) for defining our endpoint. According to these criteria, decrease in more than 25% in the postoperative GFR value as compared to preoperative period was taken as significant. This would denote only a minor RISK class. This also means that our study takes into consideration the minimum injury that has occurred to kidney. The incidence of AKI was 23.02% in our study. In other studies it was in range of 3- 30%(3–6). None of our patients had severe disease requiring dialysis in the post operative period as compared to other studies where 1-5% had severe form(71,72) There are various factors causing renal injury after CABG. Most important of them are related to the use of cardiopulmonary bypass(6). Advanced age has been described as an independent risk factor for AKI(3,6) while others have not(73,74). In our study no statistical significance was established, but following observations may show an increased incidence in older people. 4 of 21 (19.04%) patients <50 years of age developed AKI. 11of 64 (17.1%) patients in 50-60 year age group developed AKI. 14 of 41 (34.1%) patients >60 years of age developed AKI. Older patients may have a poor renal reserve and may not be able to tolerate the insults of cardiopulmonary bypass. More so older patients tend to have other co morbidities which may add to morbidity. Female sex is seen to be associated with AKI(6). The lower baseline estimated GFR observed in women could partly explain the higher incidence of AKI in female patients (75). In our study approximately 90% were males (TABLE--). Only 4 females developed AKI. The number of women is too small to draw any conclusion. DIABETES AND HYPERTENSION: The effect of DM on AKI seems to be due to renal parenchymal disease, such as glomerulonephritis(46). Glomerular filtration barrier functions as a complex biological sieve. As opposed to other capillaries in the body, glomerular capillaries are highly permeable to water and relatively impermeable to large molecules. Such permeability is possible because of the unique three-layer structure of glomerular filtration membrane consisting of endothelial glycocalyx, glomerular basement membrane, and podocytes (glomerular visceral epithelial cells). Pathological changes develop in the glomeruli of patients with long-duration DM before the appearance of microalbuminuria. The severity of glomerular damage is proportional to GFR value, DM duration, and blood glucose regulation. The main pathohistological changes in diabetic nephropathy include the thickening of the glomerular basement membrane (GBM)– Kimmelstiel-Wilson change, diffuse glomerular sclerosis, tubular interstitial fibrosis, and

arteriosclerosis and hyalinosis of kidney blood vessels (76). High blood pressure is seen to be associated with CKD. Chronic high blood pressures are more important. In our study, 54% (n=68) had diabetes, 68% (n=86) had hypertension and 43% (n=54) of the total population had both. Of the 29 patients who developed AKI 15 of them had both diabetes and hypertension. The statistical significance could not be established, but the figures do show a increased preponderance of kidney insult in these patients. STROKE: Renal function damage is associated with stroke (77). It is seen in both predialysis and dialysis patients. The risk of death increases in this subset of patients. In our study there were only 3 patients (2.38%) who had stroke in the preoperative period. None of these had renal AKI. LV DYSFUNCTION Low preoperative ejection fraction can lead to low cardiac output syndromes. This can lead to hemodynamic instability and renal hypoperfusion of kidneys to cause AKI. In our study 30% of patients had left ventricular dysfunction (LVD). Most of them had moderate LVD and mot patients who developed AKI were in this group. CPB ISCHEMIC TIME Prolonged CPB is considered as the predominant risk factor by many authors (7,46). Prolonged CPB time can cause increased systemic inflammatory response syndrome and hypoperfusion. Hemodilution and non pulsatile flow have the most deleterious effects(7,46). Pulsatile perfusion has demonstrated superior renal protection, improving organ perfusion by reducing vasoconstrictive reflexes, optimizing oxygen consumption, and reducing acidosis(78). There have been conflicting reports suggesting use of off pump CABG so as to avoid CPB induced inflammatory responses(64,79). CPB is associated with formation of free radicals, which have been shown to impair kidney function. Some have mentioned use of N-acetylcystine (NAC) which can attenuate the oxidative stress(80). Though we don't have an experience with NAC, it may be worthwhile to start using it at least in high risk patients. MEAN PERFUSION PRESSURE (MPP): CPB

7**flow rates of 1.8 to 2.** 2 litres/ **min/ m2 and a mean** arterial **pressure** above **50** to 60 **mm Hg**

are recommended(81). The following are the findings in our study: 12 of 40 (30%) patients who had a MPP <50mmHg developed AKI. 16 of 73 (21.9%) patients who had a MPP 50-60mmHg developed AKI. Only 1 of 13 (7.6%) patients who had a MPP >60mmHg developed AKI. Though no statistical significance has been obtained, the figures do show that at low perfusion pressures the incidence of AKI increases. The incidence of AKI was 4 times more when the MPP was less than 50mmHg. NO OF GRAFTS When the number of grafts increased the duration of CPB also increased, thus indirectly increasing the risk of AKI. HEMOGLBIN: Anemia prior to surgery injures kidneys by reducing the renal oxygen delivery(82). Lowest hematocrit and oxygen delivery are independent AKI predictors(83). There is progressive increase in the incidence of AKI as the post pump hemoglobin decreased in our study, but this could not attain statistical significance. 50% of patients who had Hb <6gm/dl had AKI, while only 17% patients with Hb > 8gm/dl had AKI. LACTATE BLOOD PRODUCTS As shown by various studies blood transfusion during cardiac surgery is associated with increased mortality (84,85), stroke, low cardiac output syndrome, infective complications and renal failure(86,87). We infer from our study: 5 of 40 (12.5%) patients receiving one unit of packed cells developed AKI. 8 of 24 (33.3%) patients receiving two units of packed cells developed AKI. 6 of 14 (42.8%) patients receiving more than 3 units of packed cells developed AKI. On the contrary 10 of 48 (20.8%) patients who did not receive any blood developed AKI. Incidence of AKI increased as the number of blood units transfused increases. REEXPLORATION Taking a patient for reexploration puts him at risk of anesthetic drugs, infection, risk of going on bypass again and its complications. These all can collectively lead to AKI, which may be transient. In our study only one patient was reexplored for bleeding. HOSPITAL DAYS: Increased morbidity due to AKI definitely means increased hospital stay for the patient. In our study on an average the patients were discharged on day 6 post surgery. MORTALITY We did not have any

mortality in our study. Studies have shown AKI to be independently associated with early mortality(6,71,72). PREDICTION OF AKI: Having discussed that AKI is a significant cause of morbidity in the postoperative period in CABG patients, it is important to recognise the risk prior to the procedure. Subsequently, different clinical scoring systems have been proposed(88). Chertow and colleagues(69) were among the first to developed a risk index to predict postoperative need for dialysis. However, all these proposed clinical scores had limitations including AKI etiology, duration of creatinine or GFR elevation, and recovery of renal dysfunction not being not investigated(69,89,90). WHAT ABOUT BIOMARKERS FOR PREDICTING AKI: Urea and creatinine are conventionally used to detect renal function in the post operative period. But these may not be detected early, with abnormal values coming up much later when the injury has occurred(91). The

6**Assessment, Serial Evaluation, and Subsequent Sequelae of Acute Kidney Injury (ASSESS-AKI) study and the Translational Research Investigating Biomarkers Endpoints in Acute Kidney Injury (TRIBE-AKI) study**

are ongoing prospective cohort studies, evaluating the incremental utility of novel biomarkers—cystatin C,

12**neutrophil gelatinase- associated lipocalin (NGAL), interleukin (IL)-** 6, IL-18, **kidney injury molecule-1 (KIM-1), liver-type fatty acid binding protein (L-FABP), and**

N-acetyl-_-Dglucosaminidase (NAG

6**)—to refine the diagnosis and prognosis of AKI(**

92,93). Thus AKI could be predicted and detected much before it is really causing much damage. Neutrophil gelatinase-associated lipocalin (NGAL) has been investigated extensively and would appear to be one of the most promising early AKI biomarkers(94). It measures tubular stress and is involved in the ischemic renal injury and repair process. It increases dramatically in response to tubular injury. It rises 24 hours prior to creatinine rise. LIMITATIONS OF THE STUDY

9**Statistical analysis did not show significant**

association probably

9**due to small sample size.** The number **of**

patients should have been large. This means the study should be for a longer period of time with a larger patient population. Accurate definition of renal dysfunction: there is no such perfect definition of renal dysfunction. As mentioned various studies use different methods for calculating renal dysfunction. There is

no universal definition. The comparison thus becomes difficult. This is a retrospective study. The prospective design would help in identifying more risk factors in the post operative period like the mean blood pressures in the ICU, urine output in ICU etc. Ideally creatinine clearance should be used which is a well established indicator of GFR. The use of nephrotoxic medications and inotropic support were not studied. CONCLUSION Incidence of AKI in our study is 23.02%. the incidence of AKI was 4 times more when Mean perfusion pressure was less than 50mmHg. The incidence was also higher in patients

9**more than 60 years of age.** As the number **of**

units of blood transfused increased the incidence of AKI also rises. Occurance of Acute kidney injury in patients undergoing Coronay Artery Bypass Grafting is a serious complication. It leads to longer hospital stays and thus increases the cost of treatment. Thus identifying them before irreversible injury has occurred is of paramount importance, thus improving patient prognosis. This would demand effort from clinicians and researchers for developing newer strategies and implementing the same.

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
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Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

October 11, 2013

Dr. Chengalath Manoras Mathew
Department of Cardiothoracic Surgery
Christian Medical College
Vellore 632 004

Sub: **Fluid Research grant project**:
Incidence and risk factors for acute kidney injury (AKI) in patients undergoing isolated coronary artery bypass grafting (CABG) surgery at Christian Medical College and Hospital.
Dr. Chengalath Manoras Mathew, Cardiothoracic Surgery, Dr. Alpha Mathew Kavunkal, Cardiothoracic Surgery, Dr. Roy Thankachen, Cardiothoracic Surgery.

Ref: IRB Min. No. 8378 [OBSERVE] dated 18.07.2013

Dear Dr. Chengalath Manoras Mathew,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Incidence and risk factors for acute kidney injury (AKI) in patients undergoing isolated coronary artery bypass grafting (CABG) surgery at Christian Medical College and Hospital." on July 18, 2013.

The Committee reviewed the following documents:

1. IRB Application Format
2. CV's of Drs. Chengalath Manoras Mathew, Alpha Mathew Kavunkal, Roy Thankachen.
3. Patient Consent form (English & Tamil)
4. No of documents 1- 3

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002.
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The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on July 18, 2013 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

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We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

Yours sincerely,

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ABSTRACT

TITLE OF THE ABSTRACT : **INCIDENCE AND RISK FACTORS FOR ACUTE KIDNEY INJURY (AKI) IN PATIENTS UNDERGOING ISOLATED CORONARY ARTERY BYPASS GRAFTING (CABG) SURGERY**

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DEGREE AND SUBJECT : MCh Cardiothoracic surgery

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Objectives

To study the incidence and risk factors for AKI (Acute Kidney Injury) in patients with normal preoperative renal functions undergoing CABG in CMC hospital, Vellore.

Methods

Details of 164 patients who underwent CABG between May 2013 and November 2013 were retrieved from the clinical database. From this group, all patients who had normal renal function as denoted by the preoperative creatinine and Glomerular filtration rates (GFR) were selected and their records studied.

Data would include the demographics (age, sex), kidney function prior to surgery, details of surgery (number of grafts, duration of surgery, bypass time, ischemic period, mean perfusion pressure) and post operative creatinine values.

RIFLE criteria for acute kidney injury used for the end point.

Results

The mean age was 57 years. 48.2% of those who developed AKI were >60 years of age. Males were predominant in our study. Diabetics and hypertensives had higher incidence of AKI.

The mean duration of Cardiopulmonary Bypass (CPB) in AKI group was 94.9 minutes. The mean duration of Ischemic time in AKI group was 51.93 minutes.

We could maintain a mean perfusion pressure (MPP) of 53mmHg on bypass. 41% of those developing AKI were having a MPP of <50mmHg. Blood (packed cells) was used in 78 patients (61.9%). 19(24%) of these patients developed AKI. On an average patient stayed for 6 days.

Conclusions

Incidence of AKI in our study is 23.02%. The incidence of AKI was 4 times more when Mean perfusion pressure was less than 50mmHg. The incidence was also higher in patients more than 60 years of age.

As the number of units of blood transfused increased the incidence of AKI also rises.

Occurrence of Acute kidney injury in patients undergoing Coronay Artery Bypass Grafting is a serious complication. It leads to longer hospital stays and thus increases the cost of treatment. Thus identifying them before irreversible injury has occurred is of paramount importance, thus improving patient prognosis. This would demand effort from clinicians and researchers for developing newer strategies and implementing the same.

Key words

Coronary artery bypass grafting, coronary artery disease, acute kidney injury, renal dysfunction.

INTRODUCTION

Coronary artery bypass grafting (CABG) is probably the most common adult cardiac surgery performed world over. It is a myocardial revascularization procedure used in patients having coronary artery disease (CAD). With the rise in Ischemic Heart Disease in Indian population the incidences of Coronary Artery Bypass Grafting has drastically increased. Though percutaneous interventions are on the rise CABG remains the most durable means of revascularization for coronary artery disease. It prolongs life and provides more symptomatic relief(1).

New onset acute renal failure after Coronary artery bypass grafting (CABG) is a serious complication. This can lead to significant morbidity as well as mortality. CABG is a common surgery performed at our centre. The operation includes using a cardiopulmonary bypass machine and arresting the heart using cardioplegic solution.

There are lots of vital parameter changes during and after the procedure which can lead to renal dysfunction. Though an uncommon complication after cardiac surgery, renal failure after CABG can be potentially fatal. The incidence of Acute Kidney Injury (AKI) depends on the type of cardiac surgery. The incidence is lowest after CABG, whereas it is high after valve or combined surgeries(2). This is the reason we planned to study only isolated CABG cases.

There are reports studying the risk factors causing renal injury after coronary revascularisation (3–8), but there are hardly any studies on Indian population. Christian Medical College and Hospital is a tertiary care hospital in South India. We endeavoured to study those patients undergoing CABG, who are having normal preoperative renal parameters. We would like to find out the incidence of acute kidney injury among these patients in our institute. In

addition we will also study the risk factors leading to renal dysfunction. This will help in the long run to prevent renal dysfunction in such patients.

AIMS AND OBJECTIVES

To study the incidence and risk factors for AKI (Acute Kidney Injury) in patients with normal preoperative renal functions undergoing CABG in CMC hospital, Vellore.

INCLUSION CRIETRIA:

- Patients undergoing exclusively CABG surgery in CMC Hospital.
- Patients with normal renal function prior to surgery as measured by serum creatinine.

EXCLUSION CRITERIA:

- Patients with preop renal dysfunction and having high Serum Creatinine levels.
- Redo CABG
- Patients who underwent CABG along with other cardiac procedures.
- Off pump CABG (beating heart).

MATERIALS AND METHODS

Records of patients who underwent CABG between May 2013 and November 2013 were retrieved from the clinical database. From this group, all patients who had normal renal function as denoted by the preoperative creatinine and Glomerular filtration rates (GFR) were selected and their records studied.

Details of 164 patients were collected retrospectively from the preoperative history sheet, clinical workstation and the intraoperative perfusion data sheet.

Data would include the

Demographics (age, sex)

Other important medical illness

Any medications

Kidney function prior to surgery

Details of surgery (Extent or severity of disease, Number of grafts done, duration of surgery, Bypass time, ischemic period)

Intra-operative measurements (mean perfusion pressure, blood usage)

Post-operative laboratory values.

RIFLE criteria for acute kidney injury used for the end point.

This study was approved by the IRB (Institutional Review Board) of our institute.

SURGICAL PROCEDURE:

OPERATIVE STEPS:

The chest was opened by a median sternotomy, the thymus was divided and the pericardium opened. The left anterior descending artery inspected and the left internal mammary artery was harvested in all possible cases. Simultaneously the great saphenous vein was harvested. Systemic heparinisation was done to bring the ACT to 480 sec, aortic and single two

stage venous cannulation were done and cardiopulmonary bypass was established. Marking of target vessels were done.

The Aorta was cross clamped and the heart was arrested using cold blood cardioplegia. Distal coronary anastomoses were performed using 8/0 prolene suture. Rewarming started at the completion of the last anastomosis. The cross clamp was released with root on suction. Next the proximal anastomoses were done using 6/0 prolene with side biting clamp. After coming off bypass, cannulae were removed in stages. Haemostasis was achieved. Pacing wires were taken if indicated.

Drains - Pericardial and mediastinal were inserted. Left pleural drain was inserted when left internal mammary artery was harvested. Sternum was closed with stainless steel wires followed by standard wound closure. The patient was transferred with endotracheal tube in situ to the ICU.

PERFUSION STATEGY:

All surgeries were done on pump with the heart arrested. The perfusion apparatus consisted of a custom pack of Medtronic (Affinity) or Spictra (Capiox). Nonpulsatile perfusion was used for all patients. The flow rates used for most patients were 2.2 -2.4 litres/min/m^2. Priming was done with crystalloid solution (Ringer Lactate).

ANTIBIOTICS:

All patients were given prophylactic antibiotics of Inj. Cefuroxime 25 mg/kg and Inj. Amikacin 10 mg/kg at the time of induction and followed by Inj. Cefuroxime twice daily and

Amikacin once daily for 3 days. In patients with renal dysfunction, we use Inj. Ceftazidime 25 mg/kg and Inj. Augmentin 25 mg/kg at the time of induction and thrice daily for 3 days.

In patients who develop renal dysfunction after surgery, the antibiotics are changed to Injectable Ceftazidime and Injectable Augmentin. In patients where severe infection is suspected blood cultures were taken and patients empirically started on Injectable Meropenem. When renal dysfunction was present in the post operative period, Meropenem was given in renal adjusted doses according to creatinine clearance.

POST OPERATIVE MANAGEMENT:

In the Intensive Care Unit (ICU) patients were ventilated in SIMV (synchronous intermittent mandatory ventilation) mode. The tidal volume was set at approximately 8 to 10 ml/kg. The investigations (Haemoglobin, electrolytes, cardiac enzymes, arterial blood gases, an electrocardiogram and chest Xray) are sent.

Neurological status is checked when the patient is fully awake. Sedation with either continuous morphine infusion or intermittent boluses was given. Inotropic supports were adjusted according to the hemodynamic status of the patient. Routine evaluation of serum potassium and ABG (arterial blood gases) were done in ICU. Investigations including blood urea and serum creatinine was sent everyday for 2 days.

Patients were extubated next day morning if they were hemodynamicaly stable with no complications.

The supports are tapered off on the second post operative day. All invasive lines are removed by day 3 of surgery. If satisfied patient is transferred to ward. A chest X ray and

electrocardiogram were done on the fifth postoperative day. They were discharged on the seventh or eighth postoperative day if the recovery was uneventful.

RECORD COLLECTION

Data was collected from various sources. History details were collected from the history sheet of the patient. Intra operative details were collected from the perfusion data sheet maintained in the theatre. Investigation details including all laboratory values were taken from the clinical work station on the intranet. After collection of creatinine values GFR (glomerular filtration rates) were calculated from the GFR calculator available at our CMC (Christian medical college) intranet. The Abbreviated MDRD (Modification of Diet in Renal Disease) was used for the same.

These data were entered in the Epidata software for data evaluation. With the help of the statistician these data were evaluated.

REVIEW OF LITERATURE

Coronary artery disease (CAD) is caused by obstruction to the coronary arteries. It is usually due to atherosclerotic plaque in the coronaries. Due to this plaque the internal lumen is narrowed progressively resulting in reduced myocardial blood supply. Patients may get symptoms when this blood supply is reduced.

HISTORY OF BYPASS GRAFTING:

1935 - Claude Beck reported placement of a pedicled pectoralis muscle flap on the abraded pericardium.(9)

1951 - Vineberg and Miller directly implanted the Internal Thoracic Artery (ITA) into the myocardium(Montreal)(10).

1953- Gibbon developed the cardiopulmonary bypass machine and thus the feasibility of direct coronary revascularization became possible.(11)

1954 - Murray considered direct anastomosis of Internal mammary artery to the coronaries (12).

1957 – Bailey did the first successful coronary endarterectomy(13)

1958 - Longmire reported a mammary-to coronary anastomosis. Perhaps this was the first IMA to coronary anastomosis. But actually it was performed after a surgical misadventure with a coronary endarterectomy.(14)

1962- Sabiston first reported use of a saphenous vein aorto-coronary bypass(15)

1957 - Sones & Shirey developed the coronary angiography at the Cleveland Clinic. This was considered paramount in planning an elective revascularization surgery (16).

1964 – Kolessov (Russian) is credited with the first successful planned sutured internal mammary-to-coronary anastomosis in 1964 (17)

1968 - Sen described myocardial acupuncture (18).

1971 - Effler began to revascularize using reversed saphenous vein grafts along with Favaloro based on the angiogram findings (19)

Flemma, Johnson&Lepley described advantages of sequential grafting(20)

1970 -1985 - Various randomised studies were done to compare CABG and percutaneous interventions.

The three major trials, the Coronary Artery Surgery Study (CASS)(21), the Veterans Administration Coronary Artery Bypass Cooperative Study Group(22) and the European Coronary Surgery Study (ECSS)(23) demonstrate the greatest survival benefit of revascularization.

ROLE OF ATHEROSCLEROSIS IN DEVELOPEMENT OF CAD

Fibrous plaque is formed from focal intimal lipid foci which gradually fill in the lumen to produce coronary stenosis. Complications like haemorrhage within the plaque, platelet aggregation and thrombosis cause acute MI or unstable angina. When myocardial blood flow is sufficiently impaired in relation to myocardial oxygen demands, myocardial necrosis occurs. This may lead to subendocardial ischemia or transmural necrosis. Atherosclerosis usually involves the proximal portion of major coronary arteries and the first of the secondary branches. If reperfusion occurs within 3 to 4 hours of MI, infarct size as well as mortality is reduced. Healing of the acute myocardial ischemia leaves a scarred area of myocardium. When the scar

area is almost all fibrous tissue, it is usually large and the left ventricular wall may become akinetic or anneurysmal. Repeated ischemic events may occur jeopardising function of heart.

DIAGNOSIS OF A PATIENT WITH CAD

Symptoms suggestive of angina pectoris or acute MI can help think towards CAD. ECG perhaps is the most common everyday practical test done to diagnose ischemia. Echocardiography (ECHO) will show regional wall motion abnormalities and identify left ventricular dysfunction. Angiography is the definitive and gold standard diagnostic procedure (16).

PRESENTATION

STABLE ANGINA:

Chest discomfort or pain during exercise or stress occurs because of disproportionate blood supply to the myocardial demand and reduced coronary reserve resulting from coronary atherosclerosis.

UNSTABLE ANGINA:

Severe and persisting angina with ECG changes and only minor enzymatic elevation. It is an ominous symptom. It is caused by unstable atheromatous plaque, which fissures or ruptures and sometimes a thrombus overlies.

ACUTE MI (Myocardial Infarction):

It is because of partial of complete occlusion of a coronary artery wherin the collateral blood supply is not adequate. It mostly occurs with unstable atheromatous plaques. Some patients may have repeated coronary events when the plaques are unstable. Severe proximal Left Anterior Descending artery (LAD) lesions have acute and fatal MIs.

Sudden cardiac death can result from severe myocardial ischemia resulting in ventricular fibrillation, asystole or severe LV dysfunction. Overall survival in a medically treated heterogeneous group of CAD is 75% at 5 years, 60% at 10 years and 45% at 15 years (24).

WHEN IS CABG INDICATED:(25)**:**

Asymptomatic or Mild Angina:

Class I

1. Ischemia with no symptoms/ mild angina with major left main disease.
2. Ischemia with no symptoms/ mild angina with left main Equivalent disease.
3. Ischemia with no symptoms/ mild angina with triple vessel disease.
4. No symptoms/ mild angina with disease in proximal part of LAD.
5. No symptoms/ mild angina with single or double vessel disease, but without involvement of proximal LAD.

Class IIa

1. No symptoms/ mild angina with disease in proximal LAD, with single or double vessel disease.

Class IIb

1. No symptoms/ mild angina with single or double vessel disease. These patients have no disease in proximal LAD.

Patient having stable angina

Class I

1. Stable angina with left main disease.

2. Stable angina with left main equivalent disease.

3. Stable angina with triple vessel disease.

4. Stable angina with double vessel disease with disease in proximal LAD. These also have an ejection fraction < 50% and positive noninvasive testing.

5. Stable angina with single or double vessel disease with a greater area of viable myocardium.

6. Stable angina with intolerable angina even with maximal medical management.

Class IIa

1. Stable angina with disease in proximal LAD as only a single vessel disease.
2. Stable angina with single or double vessel disease and no disease in proximal LAD.

Class III

1. Stable angina with single or double vessel disease without disease in proximal LAD.

2. Stable angina with no major coronary disease. These patients also had a negative noninvasive testing.

3. Stable angina with minor disease in coronaries.

Unstable Angina/Non–ST-Segment Elevation MI

Class I

1. Major disease in left main coronary artery.

2. Major left main equivalent disease.

3. Unstable angina or non–ST-segment elevation MI in patients. These are patients without any benefit of medical management.

Class IIa

1. Single or double vessel disease with disease in proximal LAD.

Class IIb

1. Single or double vessel disease without disease in proximal LAD. These are patients where the conditions are not favourable for percutaneous procedures.

ST-Segment Elevation MI (STEMI)

Class I

1. Need for an urgent CABG

a. Failed angioplasty and having ongoing pain

b. Ongoing pain with no response to medical management. These patients are not candidates for PCI

c. complications of septal rupture or mitral valve insufficiency

d. Cardiogenic shock

e. Life-threatening ventricular arrhythmias

Class IIa

1. Failed PCI with suitable anatomy and early presentation.

Class III

1. Persistent angina with only a small area of myocardium at risk.

Poor LV Function

Class I

1. Major left main coronary artery stenosis.

2. Left main equivalent disease.

3. Triple vessel disease involving proximal LAD.

Class IIa

1. Major viable revascularizable myocardium.

Class III

1. Without significant revascularizable viable myocardium.

Life-Threatening Ventricular Arrhythmias

Class I

1. Caused by left main coronary artery stenosis.

2. Caused by triple vessel disease.

3. Post resuscitation from sudden cardiac death or sustained ventricular tachycardia

Class IIa

1. Bypassable single or double vessel disease.

2. Disease in proximal LAD.

Class III

1. No evidence of ischemia.

CABG after failed PTCA

Class I

1. Doubt of a greater area of myocardium being jeopardised with continuing ischemia.

2. Hemodynamically unstable.

Class IIa

1. For removal of a foreign body.

2. Hemodynamically unstable with coagulation abnormalities.

Class III

1. No ischemia.

2. Not able to do a satisfactory revascularisation.

Patients with previous CABG

Class I

1. Intolerable chest pain even with maximum medical management.

2. No flow in previous done grafts and having class I indications.

PREOPERATIVE MEDICATIONS

Patients can continue beta blockers, calcium channel blocker and ACE inhibitors till the operation. There are evidence to support that preoperative beta blockers usage has decreased the postoperative atrial fibrillation(AF) (26). Digitalis can be used intraoperatively or postoperatively for rate control if there is AF. Antiplatelet agents are usually stopped 1 week prior to the surgery.

SURGERY:

The main aim of any revascularization surgery is to bypass all major and branch vessels of 1 mm or more diameter with severe stenoses (50% diameter reduction) (27). Sequential grafting may be required because of scarcity of grafts. To increase the patency of such grafting, the distal end to side anastomosis has to be done to a large vessel with tight proximal stenosis and good distal run off.

The commonly used graft strategy is anastomosis of left internal mammary artery (LITA) to left anterior descending artery (LAD). Other coronaries are grafted with saphenous vein. Radial artery grafts are used for good targets with proximal stenosis 70% or more.

Coronary angiogram provides the key information to plan CABG but on table observations will also help to decide about grafting the vessels.

WHAT ARE THE VARIOUS CONDUITS FOR REVASCULARISATION?

VENOUS GRAFTS

Venous grafts are commonly taken from the legs; usually the great saphenous vein is used. Most centres over the world use saphenous vein in most of the patents. Therefore in reoperations alternate conduits like the short saphenous vein, right internal thoracic artery, radial artery, right gastroepiploic and in rare cases cephalic vein, splenic artery and ulnar arteries may be used. Varicose veins are unsuitable as graft conduits, whereas superficial varicosities are not.

TECHNIQUE OF HARVESTING SAPHENOUS VEIN:

The legs are abducted and knees are flexed about 45°. Incision is made anterior to medial malleolus to harvest lower segment, whereas groin incision is made for upper segments and

extended according to the length needed. Care is taken not to create flaps while harvesting the vein so as to prevent skin necrosis. The saphenous nerve is also preserved. External diameter of 3 to 3.5 mm is considered satisfactory. A single long segment of great saphenous vein of about 50 to 65cm is harvested. Usual requirement for diagonal graft is 12 to 15 cm of vein length, whereas for marginal grafts (20 to 24 cm) and right coronary artery and its branch grafts (18 to 22 cm) will be needed. The branches are ligated or clipped just flush with the vein wall to avoid diverticula or luminal narrowing. The subcutaneous tissue and skin are sutured subsequently.

To harvest the short saphenous vein, patient is placed in prone position and incision is started posterior to the lateral malleolus. Here the sural nerve is preserved which runs parallel to it. After dividing the vein subcutaneous tissue and skin are sutured.

Endoscopic vein harvesting can also be done. This reduces pain and wound complications, but is more time consuming than the conventional method.

The harvested vein is distended with solution; the leaking branches looked for and are clipped or ligated. It is advisable to preserve this harvested venous graft in balanced salt solution to prevent endothelial damage till we anastomose it (28).

ARTERIAL GRAFTS:

Internal Mammary Artery (Internal Thoracic Artery) (IMA/ITA):

Usually the left IMA is harvested as a choice of graft to the Left Anterior Descending Coronary Artery. It is mobilised after sternotomy. There are standard sternal retractors which help to elevate left sternal edge and thus the left internal thoracic artery is exposed. It can be harvested as skeletonised or pedicled graft.

Incision is made medial to the IMA using low power electrocautery and extended along the whole length. The pleura may be widely opened to get better exposure. Nevertheless extra pleural harvesting can also be done. The phrenic nerve is to be carefully dealt with and preserved at the proximal end. With slight traction, intercostal branches can be identified, clipped and divided.

After heparinisation, the distal end is divided. The IMA is checked for good flow. It is wrapped in gauze soaked with papavarine solution till heart is taken on bypass. Once the distal anastomosis with the vein grafts are finished, the IMA is anastomosed to LAD using 7-0 or 8-0 polypropylene suture.

The IMA can be sequentially grafted to diagonals and LAD. Skeletonization preserves the sternal blood supply. Thus it is preferable in conditions where the risk of infection is high like obesity, diabetes and bilateral internal thoracic artery harvesting.

Radial Artery:

The prerequisite for using the radial artery is that the palmar arch should be intact. The best way of making it sure is the by doing the Allen's test. It is performed in the non dominant hand before surgery to make sure that palmar arch gets supply from the ulnar artery after removing the radial artery. The patient is asked to clinch his fist for 30 seconds. The radial and ulnar arteries are occluded with fingers. The hand is opened now and the palm will be seen to be blanched. On releasing the occlusion on the ulnar artery, the palm should become flushed within 5 to 6 seconds. This denotes adequate blood supply to the palmar arch by the ulnar artery and a negative Allen's test.

The arm is positioned by the side. A separate draping is done. Incision is made over the radial pulse in the wrist and extended proximally. Dissection is done and the branches are clipped and divided. The artery is removed after ligating both ends. The artery is irrigated and dilated with ringer lactate solution containing heparinised blood and sodium nitroprusside. Radial artery is known to undergo spasm. The irrigation is done to prevent this spasm. The artery is immersed in the same solution until it is anastomosed.

Right Gastroepiploic Artery (GEA):

The Midline sternotomy incision is extended upto the point midway between xiphisternum and umbilicus. The abdomen is entered and the liver is retracted to the right side. Right GEA branches are ligated and divided along the greater curvature for required length. The pedicle is passed either anterior or posterior to the duodenum, then through a diaphragmatic opening made medial to the inferior venacava opening. Though this graft can be used to bypass most of the coronary arteries, it is commonly used to graft the distal RCA or Posterior Descending Artery (PDA).

Inferior Epigastric Artery (IEA):

It is harvested through a paramedian incision. It originates from external iliac artery along the medial edge of deep inguinal ring. It then ascends obliquely toward the umbilicus. It has a mean length of 13 cm and a mean diameter of 2.4 mm. The artery is wrapped in gauze soaked in papaverine and immersed in the same solution until it is used.

Splenic Artery:

It is used rarely when other conduits are not available. Midline sternotomy is extended down to a point midway between xiphisternum and umbilicus. The lesser sac is opened. The splenic artery branches to pancreas are ligated and divided. The artery is divided at the hilum. Splenectomy is not needed as it is supplied by short gastric branches of left gastric artery also. The splenic artery is passed through a diaphragmatic opening made medial to the inferior vene cava and anastomosed to branches of RCA and LCX.

DISTAL ANASTOMOSES:

The epicardium over the selected coronary vessel is marked. Clearing of the anterior surface of the artery is done gently with the help of scalpel. The anterior wall of the artery is opened with sharp blade slightly obliquely to prevent opening of posterior wall. Arteriotomy is extended on both sides to a length of 4 to 6 mm. The end of the venous conduit is bevelled and incision is made to make opening 10 to 20% larger than the arteriotomy. The sutures are placed little away from the margin in the vein. The coronary artery suture pierces the intima near the edge and comes out several millimetres away from edge. The stitches are placed separately. The double armed sutures are started at one corner of the arteriotomy and continued either clockwise or anticlockwise to tie with the other arm of the suture.

For sequential anastomoses, if the vein is of adequate size, it can be opened perpendicular to the long axis. The incision should not exceed one third of the circumference. The anastomosis is begun in the middle of the venous opening and continued around and tied. If the vein is small or if radial artery or ITA is used, it is opened parallel to its long axis. The

diamond anastomosis is made. After each anatomosis, the conduit is distended to avoid excess length or tension between sequential anastomosis.

PROXIMAL ANASTOMOSES:

After releasing the aortic cross clamp, a partially occluding side biting clamp is applied on the ascending aorta. Hole is made in the aorta using aortic punch. Conduits are positioned in such a way that they are not kinked or tense. The proximal end is cut obliquely and incised to create a circumference 10 to 20% larger than aortic opening to form cobra head at the completion of anastomosis. A double armed 6-0 polypropylene suture is used for the anastomosis. If the aorta is severely calcified, proximal anastomosis can be done without side biting clamp, while the heart is still arrested. During off pump coronary artery bypass surgery, proximal anastomosis is done before distal anastomosis.

MANAGEMENT IN THE POSTOPERATIVE PERIOD

EARLY:

It is advised to start Aspirin 150 mg, as soon as the chest drainage settles, preferably within first 6 hours of surgery and continued once daily thereafter to enhance the vein graft patency(29).

Oral beta blocker is given 4 to 6 hours postoperatively. This is balanced against ionotrope use in the ICU. Ideally it is continued as a prophylaxis against supraventricular arrhythmias (30). Digitalis is not routinely used because it may produce atrial and ventricular arrhythmias.

The patients may develop 10 to 20 % fall in blood pressure 8 to 12 hours after surgery with good pedal pulses and cardiac index >2. Some patients may require low dose dopamine (3.5 mics/kg/min).

Intra Aortic Balloon Pump is occasionally required for patients who have low cardiac output with high left atrial pressure or presence of intractable ventricular arrhythmias intraoperatively or in the immediate postoperative period.

LATE:

CABG is only a palliative procedure. It only ensures revascularisation. But it is par essential to educate patients about their condition so as we as clinicians ensure the graft is patent for a long time.

The most powerful predictor of survival is the use of LIMA TO LAD.

Aspirin should be administered immediately after surgery and continued for at least 1 year postoperatively is the well established effective regimen (31).

Control of atherosclerosis risk factors retards and even reverse atherosclerosis in the vein grafts.

Smoking must be stopped.

Body weight should be maintained, special dieting is followed if required. Hypertension and saturated fat in diet must be controlled. Serum lipids must be maintained within normal limits either with diet or drugs (32,33).

SURVIVAL:

The survival rates after isolated CABG are 98% at 1 month, 97% at 1 year, 92% at 5 year, 81% at 10 year and 66% at 15 year or more (34)

MORBIDITY:

NEUROLOGICAL:

Postoperative neurological deficit is the important cause for morbidity and mortality. The incidence may be approximately 5 to 6%. There are two types(35).

Type I deficit – major focal deficits, stupor, and coma. It accounts for 3.1%. The predictors are aortic atherosclerosis, previous history of neurological disease, use of intra aortic balloon pump (IABP), diabetes.

Type 2 deficit – deficit in intellectual and memory. It accounts for 3%.

MEDIASTINITIS:

It is one of the devastating complications to occur. Deep sternal wound infection seen in < 5% of patients who undergo CABG with CPB and increases the mortality (36). Obesity is a risk factor. Other risk factors are diabetes mellitus, previous CABG and use of both IMAs.

RENAL DYSFUNCTION:

This topic is taken up separately at the end of review of literature. Renal dysfunction increases the mortality from 0.9% (without renal impairment) to 1.9% (with renal impairment). The preoperative risk factors are advanced age, moderate to severe cardiac failure, previous CABG, diabetes mellitus & previous renal disease. This complication was similar in both CABG groups with and without CPB in many studies.

INCREMENTAL RISK FACTORS FOR DEATH:

Most deaths after CABG are from cardiac failure. About 25% of deaths are not related to coronary artery disease or the operation(37). It is paramount to understand these factors.

PATIENT SPECIFIC:

AGE:

Older age is a risk factor for prolonged hospital stay and early complications.

SYMPTOMS OF ISCHEMIA:

Canadian angina class and unstable angina grade, higher the grade the risk is increased.

NONCARDIAC COMORBIDITY:

Various noncardiac factors may play in increasing the morbidity. Obesity, hypertension, diabetes mellitus, hypertriglyceridemia, history of smoking, low FEV1 %, history of peripheral vascular disease, or a history of surgery for the same, history of cerebrovascular disease and renal failure are all risk factors for early death after CABG (38).

CARDIAC COMORBIDITY:

Associated cardiac conditions such as mitral regurgitation, aortic regurgitation, atrial fibrillation, ventricular arrythmias and requirement of a cardiac pacemaker increase the postoperative morbidity and mortality.

LEFT VENTRICULAR FUNCTION:

Patients who presents with cardiogenic shock after myocardial infarction, higher NYHA class limiting the activity and low ejection fraction will adversely affect the outcome after surgery. The presence of low ejection fraction associated with mitral regurgitation increases the risk above that of low ejection fraction alone.

CONCOMITANT PROCEDURES:

Left ventricular reconstructive procedures will increase the mortality rate.

QUALITY OF LIFE:

Most of the patients get a good quality of life. This good quality gradually declines 5 years post surgery.

The use of arterial line filters has reduced the incidence of neurobehavioral and cognitive dysfunction. Prevalence is affected by pre and post operative anxiety, depression and old age. Gross deficits result from embolisation of ascending aortic atherosclerotic debris, air or intracardiac thrombus rather than CPB effects. Prevalence is roughly 0.5% in young,, but raises to 5% in older people and about 8% in patients over 75 years(38).

Almost all studies show a decrease in the use of beta blocker and vasodilator medications after CABG. Maximal exercise capacity is also improved by CABG and ECG abnormalities are importantly reduced.

GRAFT PATENCY:

INTERNAL THORACIC ARTERY:

IMA is an excellent conduit for CABG.

About 90% of the left IMAs anastomosed to LAD are patent at 10 to 20 years after operation and closure after that is uncommon. However 5 to 10% of grafts have stenoses late postoperatively, most of which do not progress to occlusion.

Various factors favour the excellent performance of IMA. It is partially because of continued functioning of endothelial cells, which secretes endothelial derived relaxing factor and prostacyclin. It has inherent property to resist development of atherosclerosis. Another important factor in grafting to LAD is the large runoff through the diagonal and septal branches.

It has been seen that use of bilateral ITAs increases survival. But wound complications are more common particularly in obese and diabetic patients when bilateral IMA is harvested.

RADIAL ARTERY:

Early patency of radial artery exceeds 90%. Native coronary artery stenosis of less than 70% reduces the patency rate (39).

GASTROEPIPLOIC ARTERY:

Its early patency rate within one year is 94%, between 1 and 5 years is 88% and between 5 and 10 years is 83% (40).

INFERIOR EPIGASTRIC ARTERY:

Early patency was 98% and late patency was 93%. Graft patency is improved when anastomosed to a vessel with proximal occlusion of 60% or more(41).

SAPHENOUS VEIN GRAFT:

Intimal hyperplasia is found universally in venous grafts after 1 month of surgery. This process is not progressive. Thickness of the hyperplasia is inversely proportional to the flow rate, so it is considered as a remodelling process. Atherosclerotic lesions may not be found in grafts of less than 3 ½ years duration. By 10 years, most of the grafts have some atherosclerotic changes sometimes severe in nature. Whether these changes result from morphological damage during harvest and insertion or by patient's tendency or by both is uncertain. Hyperlipidemia is a risk factor for extensive vein graft atherosclerosis. Thrombosis of venous grafts can reduce the patency early postoperatively which results from endothelial loss and exposure of basement membrane to blood. It can also develop late in heavily atherosclerosed areas. Because of these reasons 10% of graft closure occurs within few postoperative weeks, particularly when antiplatelets are not used.

Lesser saphenous vein patency rate appears to be equal to the great saphenous vein. Upper limb veins have lower patency rates. When there is unavailability of these veins, cryopreserved allograft veins can be used, which have very low late patency rates.

CABG AND RENAL FAILURE

Acute kidney injury (AKI) is loss of kidney function precipitously. Urea is accumulated and so are the nitrogenous compounds. Initially well known as acute renal failure (ARF) now the

term AKI is used. ARF term should be used for severe AKI, usually when a form of renal replacement is required.(42)

Several definitions of AKI have been developed in order to provide a uniform definition of AKI. In 2004, the Acute Dialysis Quality Initiative (ADQI) group gave guidelines management of AKI. When they felt the great need for a standard definition for AKI, they proposed the RIFLE criteria (43).

A modification of the RIFLE criteria was later given by Acute Kidney Injury Network (AKIN) (44)

We have followed the RIFLE criteria in our study.

RIFLE CRITERIA

RIFLE gives 3 grades of increasing severity for any form of acute injury to kidneys – risk (class R), injury (class I) and failure (class F) – and two outcome classes (loss and end-stage kidney disease)(45). A unique feature of the RIFLE classification is that it provides three grades of severity for acute kidney injury based on changes in either serum creatinine or urine output from the baseline condition. This allows classification of patients with acute kidney injury into one of the three RIFLE severity classes.

- Risk — 1.5-fold increase in the serum creatinine, **or** glomerular filtration rate (GFR) decrease by 25 percent, **or** urine output <0.5 mL/kg per hour for six hours

- Injury — Twofold increase in the serum creatinine, **or** GFR decrease by 50 percent, **or** urine output <0.5 mL/kg per hour for 12 hours
- Failure — Threefold increase in the serum creatinine, **or** GFR decrease by 75 percent, **or** urine output of <0.3 mL/kg per hour for 24 hours, **or** anuria for 12 hours
- Loss — Complete loss of kidney function (eg, need for renal replacement therapy) for more than four weeks
- ESRD — Complete loss of kidney function (eg, need for renal replacement therapy) for more than three months

The change in serum creatinine was specified as occurring over not more than seven days.

PATHOGENESIS OF AKI:

The development of postoperative AKI is usually due to various preoperative, intraoperative and postoperative factors. The preoperative factors are usually patient related. The intraoperative factors mostly due the CPB and the surgery per se. (7,46,47).

Kidneys are prone to ischemic damage. Renal arteries are endarteries. There are some effects of CPB that can cause renal injury. These alterations may be in the blood flow, low cardiac output, hemodilution, renal vasoconstriction, and loss of pulsatile flow during CPB (7,46,48). These factors causes an imbalance in oxygen supply/demand to the kidney causing cellular injury (49,50).

There is a correlation between hypothermia during CPB and AKI (51,52). The causative mechanism seems to be related to the increased metabolic demand with the subsequent nephron

damage due to low perfusion temperatures as the result of hypoperfusion of the superficial cortex that occurs during rewarming and restoration of normothermia (51).

The CPB-induced systemic inflammatory response is an important cause of renal injury. It causes interstitial inflammation with tubular injury(53,54). During CPB the blood cells are exposed to nonphysiologic surfaces leading to cell lysis (55). These destroyed red blood cells release plasma free hemoglobin into the circulation causing occlusion of renal tubules with hemoglobin casts and necrosis of tubular cells (55).

Last but not the least CPB causes embolization of particulate matter (56). Studies have shown that emboli counts were independently associated with postoperative AKI (57).

AKI is an accepted serious complication after coronary revascularisation. This increases morbidity and mortality. The stay in hospital is also increasesd(58). The risk of Acute Kidney Injury (AKI) varies from 3-30% (58,59). The mortality rates increases when AKI leads to requirement of dialysis.

MODIFICATION OF DIET IN RENAL DISEASE FORMULA(60)

The MDRD equation was developed in 1999. The Cockcroft-Gault formula estimates creatinine clearance. MDRD study estimates GFR by measuring ^{125}I-iothalamate urinary clearance. The values were taken from patients with established CKD.

There are many MDRD equations. The more commonly used one is the abbreviated (four-variable) MDRD equation. Age, sex, racial factor are all used.

Glomerular Filtration Rate (GFR) Equations

- Cockcroft-Gault formula = ([140 − age] × weight)/(72 × SCr)

(Multiply by 0.85 if female; expressed in mL/min.)

- Abbreviated MDRD equation = $186 \times (SCr^{-1.154}) \times (age^{-0.203})$

(Multiply by 0.742 if female, by 1.212 if African American; expressed in mL/min/1.73 m^2)

THE DEBATE ON TAKING A LOWER GFR VALUE AS NORMAL FOR INDIAN POPULATION:

A normal reference range for glomerular filtration rate (GFR) in adult Indian potential kidney donors has not been determined. The values from a western population are being used as reference. On the whole population in India has a lower body surface area as compared to the west. Thus it is important to understand that the GFR values which fall in mild renal dysfunction may be normal for Indian population.

The normal GFR for an Indian is considerably lower than western population(61). The mean GFR would be 81.4 ± 19.4 ml/min/1.73 m^2 BSA, which is much lower than the normal value of 110–120 ml/min derived from a western population.

Various Indian studies take in the value of GFR of approximately 60ml/min/1.73m^2 as normal for Indian population(62,63). We have also taken normal GFR as 60ml/min/1.73m^2 for our study.

RESULTS

We studied 164 consecutive patients between May 2013 and November 2013. These 164 patients had a normal creatinine value prior to surgery. The normal creatinine value defined by our CMC biochemistry laboratory is 1.4mg/dl. Of these patients only 126 patients had a normal GFR. The normal GFR was taken as 60ml/min/1.73m^2 for our Indian population(62,63). There were 126 patients that satisfied these criteria.

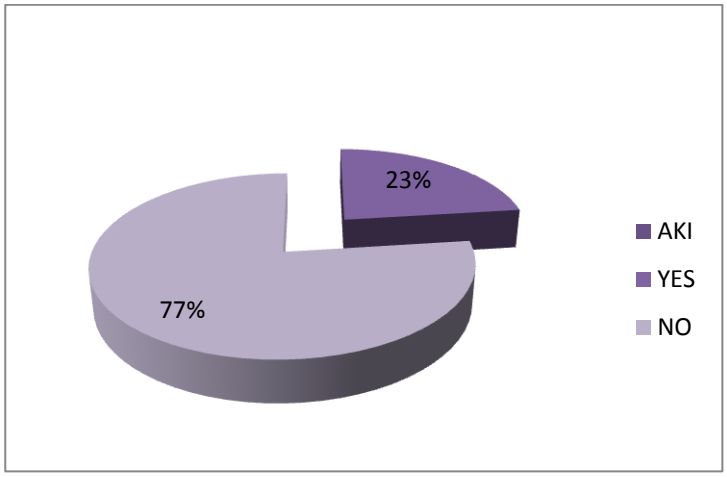
We studied the risk factors for AKI in 3 parts – preoperative, intraoperative and postoperative factors. We studied factors in general population of patients as well as in two groups, i.e. one group which developed Acute Kidney Injury (AKI) and the other which did not develop AKI. A GFR reduction of >25% was taken as class R Acute Kidney Injury (rifle criteria). The incidence of AKI in our study was 23.02%.

The general demographics are as below:

Variable	Mean	Std. Dev.	Min	Max
age	57.26	6.97	33	73
weight	63.27	9.85	38	89
Preop_creatinie	1.08	0.15	0.74	1.76
Preop_gfr	73.45	10.99	60.12	99.98
Tpt (Total pump time)	92.38	25.78	31	163
Ischemic time	48.30	12.73	19	83
mean perfussion pressure	53.22	5.68	40	73
Post pump hemoglobin	10.45	1.04	8.1	13.4

Variables	Groups	N	%
Sex	male	113	89.68
	female	13	10.32
Diabetes	yes	68	53.97
	no	58	46.03
Hypertension	yes	86	68.25
	no	40	31.75
Copd	yes	1	0.79
	no	125	99.21
Stroke	yes	3	2.38
	no	123	97.62
lvd	yes	39	30.95
	no	87	69.05

AKI	N	%
YES	29	23.02%
NO	97	76.98%

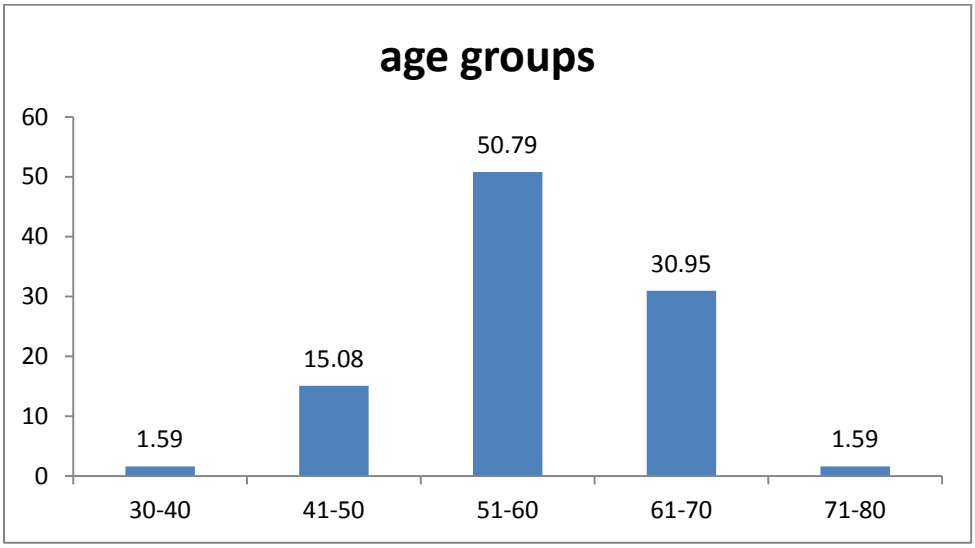


PREOPERATIVE FACTORS:

AGE:

The mean age in our study was 57 years with the youngest being 33 and oldest being 73. Most patients were between 51-60 years. The age distribution is shown below:

Age	Freq.	Percent
30-40	2	1.59
41-50	19	15.08
51-60	64	50.79
61-70	39	30.95
71-80	2	1.59



48.2% of those who had GFR reduction were >60 years of age. Though a causal relationship could not be established, it seems AKI is more prone in older age.

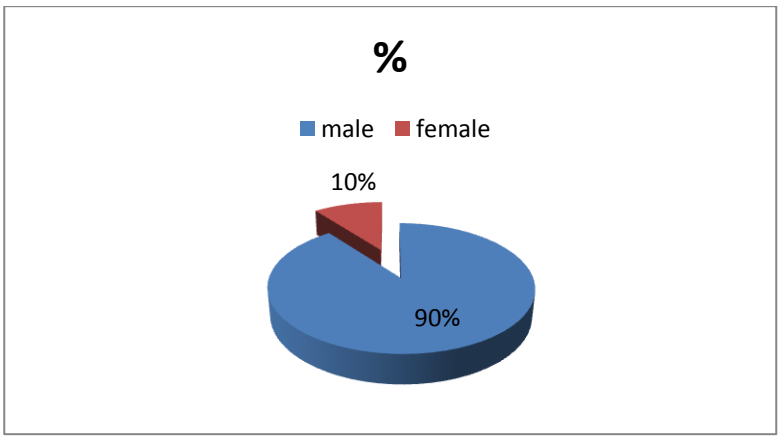
Variables	Groups	gfr_red			p-value
		No	Yes	Total	
Age	<=50	17	4	21	0.118

	%	17.53%	13.79%	16.67%	
	51-60	53	11	64	
	%	54.64%	37.93%	50.79%	
	>=61	27	14	41	
	%	27.84%	48.28%	32.54%	
Total		97(76.98%)	29(23.02%	126(100%)	

SEX:

Males were predominant in our study. There were 113(89.68%) males and 13(10.32%) females.

Variables	Groups	N	%
Sex	male	113	89.68
	female	13	10.32



The following is the table which shows the average males and females in the two groups of AKI and non AKI:

Variables	Groups	gfr_red			p-value
		No	Yes	Total	
Sex	Male	88	25	113	0.483
	%	90.72%	86.21%	89.68%	
	Female	9	4	13	
	%5	9.28%	13.79%	10.32%	

86.2% (n=25) of AKI patients were men, but the total number of women in the study (n= 13) was too small to draw any conclusions.

DIABETES AND HYPERTENSION:

There were 68 patients with diabetes (DM) and 86 patients had hypertension (HT), while 54 patients had both. The incidence of AKI in patients with both DM and HT was found to be higher.

Variables	Groups	n	%
Total Diabetes	yes	68	53.97
	no	58	46.03
Total Hypertensives	yes	86	68.25
	no	40	31.75

Variables	Groups	gfr_red			p-value
		No	Yes	Total	
ht_dm	no	21	5	26	0.676
		21.65	17.24	20.63	
	ht	25	7	32	
		25.77	24.14	25.4	
	dm	12	2	14	
		12.37	6.9	11.11	
	both	39	15	54	
		40.21	51.72	42.86	

STROKE:

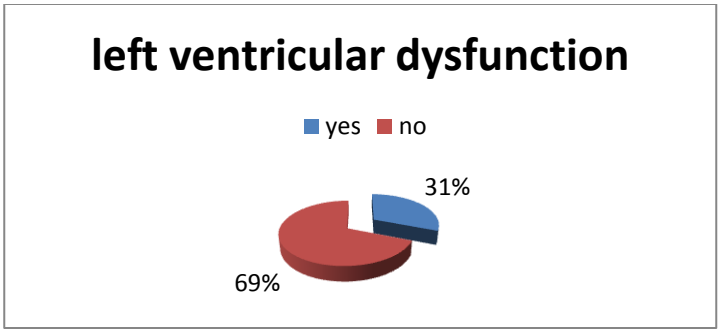
Three patients had stroke prior to study. None of these patients developed AKI.

LEFT VENTRICULAR DYSFUNCTION:

12 of 29 patients who developed AKI had left ventricular dysfunction.

Variables	Groups	N	%

Lvd	yes	39	30.95
	No	87	69.05



Of the lvd group, there were only 2 patients with severe LVD (<30%), and roughly 72% of had moderate LVD (31-45%). Only 23% had mild LVD. AKI was seen more in moderate LVD group. No association was found in patients with severe LVD.

Variables	Groups	gfr_red			p-value
		No	Yes	Total	
LVD	<=30	2	0	2	0.625
		7.41	0	5.13	
	31-45	19	9	28	
		70.37	75	71.79	
	>=46	6	3	9	
		22.22	25	23.08	

PREOPERATIVE CREATININE VALUES:

Preoperatively the mean creatinine of the study was 1.13 mg/dl

PREOPERATIVE GFR VALUES:

The mean preoperative GFR was 73 ml/min/1.73m$^{2.}$ The least and maximum values being 60 and 90ml/min/1.73m^2 respectively.

PREOPERATIVE HEMOGLOBIN AND LACTATE VALUES:

The mean preoperative haemoglobin was 12gm/dl, whereas the mean lactate values were 1.29millimoles/L.

INTRAOPERATIVE FACTORS:

DURATION OF CARDIOPULMONARY BYPASS:

The mean duration of Cardiopulmonary bypass (CPB) of the whole group was 92 minutes (range 31 – 163 minutes). Whereas the mean Ischemic time (the cross clamp time) was 48 minutes (range 19-83 minutes).

The mean duration of CPB in AKI group was 94.9 minutes. This was greater than the group having no AKI.

	n	mean	sd	min	median	max	p-val
No GFR reduction	97	91.64	25.3	31	94	163	
GFR reduction	29	94.9	27.64	48	98	150	0.55

The mean duration of Ischemic time in AKI group was 51.93 minutes. There was no statistical significance between these groups.

	n	mean	sd	min	median	max	p-val
No GFR reduction	97	53.61	5.76	40	54	73	
GFR reduction	29	51.93	5.34	42	52	66	0.16

MEAN PERFUSION PRESSURE: (MEAN ARTERIAL PRESSURE):

The entire group had a mean perfusion pressure of 53mmHg (range 40-73mmHg). Though 41% of those developing AKI were having a mean perfusion pressure of <50, a causal relationship could not be established statistically.

Variables	Groups	gfr_red			p-value
		No	Yes	Total	
MPP	<=50mmHg	28	12	40	0.238
	%	70%	30%	100%	
	50-60mmHg	57	16	73	
	%	78.1%	21.9%	100%	
	>=61mmHg	12	1	13	
	%	92.4%	7.6%	100%	

30% (12/40) patients with perfusion pressure (MPP) less than 50mmHg developed AKI, while only 7.6 %(1/13) patients with MPP >61 had AKI.

The incidence of AKI was 4 times more when the MPP less than 50mmHg.

NUMBER OF GRAFTS:

Most of patients who had renal dysfunction had 3 grafts (64%). Only 8(27%) of 29 patients who were grafted with 4 vessels developed AKI. Thus the number of grafts may not be a major factor in causing AKI. More number of grafts means more the duration of CPB.

POST BYPASS HEMOGLOBIN:

The mean post bypass haemoglobin was 8.0gm/dl (range: 5.6 – 10.5). .

There were only 2 patients with post pump haemoglobin <8gm/dl and one (50%) developed AKI.

There were 70 patients with post pump haemoglobin >8gm/dl and 12 (17.1%) of them developed AKI.

There was progressive increase in incidence of AKI as post pump haemoglobin decreases. There was no statistical significance found.

post_phb		GFR_red		p-val
		NO	YES	
<8	n	39	17	
	%	40.21	58.62	
>=8	n	58	12	
	%	59.79	41.38	0.08

POST BYPASS LACTATE:

The average post bypass lactate was 3.35millimoles/L.

12 of 53 (22.6%) patients having lactate levels of <3millimoles/L developed AKI.

7 of 39 (17.9%) patients having lactate levels between 3-4millimoles/L developed AKI.

10 of 34 (29.4%) patients having lactate levels >4millimoles/L developed AKI.

	Groups	GFR reduction	No GFR redction	total	P value
Post pump lactate	<= 3	41(77.4%)	12(22.6%)	53(100%)	0.508
	3.1-4.0	32(82.1%)	7(17.9%)	39(100%)	
	>=4	24(70.6%)	10(29.4%)	34(100%)	

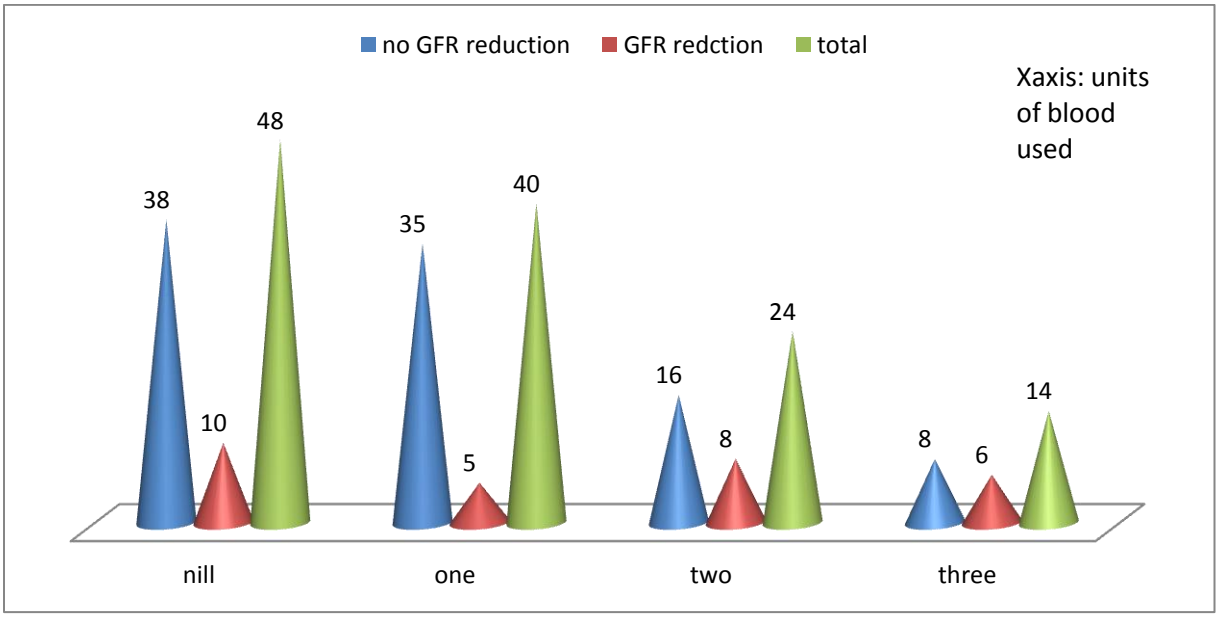
Increased incidence (29.4%) AKI with post bypass lactate levels of >4 mmol/l was seen.

BLOOD PRODUCTS:

Blood (packed cells) was used in 78 patients (61.9%). 19(24%) of these patients developed AKI.

The incidence of AKI increased as the number of units of blood transfused increased. Those transfused with more than 3 units of blood had more than three times the incidence of AKI compared to those who had only one unit transfused. A statistical significance was not achieved though

Variables	Groups	gfr_red			p-value
		No	Yes	Total	
PRODUCTS WB	0	38	10	48	0.066
		79.2%	**20.8%**	100%	
	1	35	5	40	
		87.5%	**12.5%**	100%	
	2	16	8	24	
		66.7%	**33.3%**	100%	
	>=3	8	6	14	
		57.2%	**42.8%**	100%	



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ULTRAFILTRATION:

Was done only in one patient.

RETROGRADE AUTOLOGOUS PRIMING (RAP):

Overall 30 (23%) patients underwent RAP.

Variables	Groups	n	%
rap	Yes	30	23.81
	No	96	76.19

20% of patients who underewent RAP developed AKI; wheras 33% of those who did not undergo RAP developed AKI.

		GFR reduction		
RAP		NO	YES	p-val
YES (TOTAL 30)		25	5(20%)	
NO (TOTAL 96)		72	24(33%)	
				0.344

POSTOPERATIVE FACTORS:

REEXPLORATION:

There was only one re-explorations done for increased postoperative drainage.

***DIALYSIS*:**

None of the patients were dialysed in the postoperative period.

HOPSITAL STAY:

The mean duration of postoperative stay was 6 days.

MORTALITY:

Only one patient died of recurrent ventricular fibrillation.

DISCUSSION:

Definitions of renal dysfunction have been used varyingly in literature. Some have used absolute values of postoperative cut off creatinine values as 1.5mg/dl (64,65), as >2.1mg/dl (6), as doubling of baseline creatinine values (3,66) while some have used creatinine clearance of <50ml/min (67)as a marker. Various formulas of estimated Glomerular Filtration Rate (GFR) like Cockroft-Gault formula for Creatinine Clearance (5,68) and the Modification of Diet in Renal Disease (MDRD) formula for Estimated Glomerular Filtration Rate (eGFR) has been used. Others have also defined AKI as only when a deterioration in renal function requires dialysis(69,70)

We used the abbreviated MDRD formula for calculation of GFR. We also used the RIFLE criteria (45) for defining our endpoint. According to these criteria, decrease in more than 25% in the postoperative GFR value as compared to preoperative period was taken as significant. This would denote only a minor RISK class. This also means that our study takes into consideration the minimum injury that has occurred to kidney.

The incidence of AKI was 23.02% in our study. In other studies it was in range of 3-30%(3–6). None of our patients had severe disease requiring dialysis in the post operative period as compared to other studies where 1-5% had severe form(71,72)

There are various factors causing renal injury after CABG. Most important of them are related to the use of cardiopulmonary bypass(6).

Advanced **age** has been described as an independent risk factor for AKI(3,6) while others have not(73,74). In our study no statistical significance was established, but following observations may show an increased incidence in older people.

4 of 21 (19.04%) patients <50 years of age developed AKI.

11of 64 (17.1%) patients in 50-60 year age group developed AKI.

14 of 41 (34.1%) patients >60 years of age developed AKI.

Older patients may have a poor renal reserve and may not be able to tolerate the insults of cardiopulmonary bypass. More so older patients tend to have other co morbidities which may add to morbidity.

Female **sex** is seen to be associated with AKI(6). The lower baseline estimated GFR observed in women could partly explain the higher incidence of AKI in female patients (75). In our study approximately 90% were males (TABLE--). Only 4 females developed AKI. The number of women is too small to draw any conclusion.

DIABETES AND HYPERTENSION:

The effect of DM on AKI seems to be due to renal parenchymal disease, such as glomerulonephritis(46).

Glomerular filtration barrier functions as a complex biological sieve. As opposed to other capillaries in the body, glomerular capillaries are highly permeable to water and relatively impermeable to large molecules. Such permeability is possible because of the unique three-layer structure of glomerular filtration membrane consisting of endothelial glycocalyx, glomerular

basement membrane, and podocytes (glomerular visceral epithelial cells). Pathological changes develop in the glomeruli of patients with long-duration DM before the appearance of microalbuminuria. The severity of glomerular damage is proportional to GFR value, DM duration, and blood glucose regulation. The main pathohistological changes in diabetic nephropathy include the thickening of the glomerular basement membrane (GBM)–Kimmelstiel-Wilson change, diffuse glomerular sclerosis, tubular interstitial fibrosis, and arteriosclerosis and hyalinosis of kidney blood vessels (76).

High blood pressure is seen to be associated with CKD. Chronic high blood pressures are more important.

In our study, 54% (n=68) had diabetes, 68% (n=86) had hypertension and 43% (n=54) of the total population had both. Of the 29 patients who developed AKI 15 of them had both diabetes and hypertension. The statistical significance could not be established, but the figures do show a increased preponderance of kidney insult in these patients.

STROKE:

Renal function damage is associated with stroke (77). It is seen in both predialysis and dialysis patients. The risk of death increases in this subset of patients.

In our study there were only 3 patients (2.38%) who had stroke in the preoperative period. None of these had renal AKI.

LV DYSFUNCTION

Low preoperative ejection fraction can lead to low cardiac output syndromes. This can lead to hemodynamic instability and renal hypoperfusion of kidneys to cause AKI.

In our study 30% of patients had left ventricular dysfunction (LVD). Most of them had moderate LVD and mot patients who developed AKI were in this group.

CPB ISCHEMIC TIME

Prolonged CPB is considered as the predominant risk factor by many authors (7,46). Prolonged CPB time can cause increased systemic inflammatory response syndrome and hypoperfusion. Hemodilution and non pulsatile flow have the most deleterious effects(7,46). Pulsatile perfusion has demonstrated superior renal protection, improving organ perfusion by reducing vasoconstrictive reflexes, optimizing oxygen consumption, and reducing acidosis(78).

There have been conflicting reports suggesting use of off pump CABG so as to avoid CPB induced inflammatory responses(64,79). CPB is associated with formation of free radicals, which have been shown to impair kidney function. Some have mentioned use of N-acetylcystine (NAC) which can attenuate the oxidative stress(80). Though we don't have an experience with NAC, it may be worthwhile to start using it at least in high risk patients.

MEAN PERFUSION PRESSURE (MPP):

CPB flow rates of 1.8 to 2.2 litres/ min/ m^2 and a mean arterial pressure above 50 to 60 mm Hg are recommended(81). The following are the findings in our study:

12 of 40 (30%) patients who had a MPP <50mmHg developed AKI.

16 of 73 (21.9%) patients who had a MPP 50-60mmHg developed AKI.

Only 1 of 13 (7.6%) patients who had a MPP >60mmHg developed AKI.

Though no statistical significance has been obtained, the figures do show that at low perfusion pressures the incidence of AKI increases. The incidence of AKI was 4 times more when the MPP was less than 50mmHg.

NO OF GRAFTS

When the number of grafts increased the duration of CPB also increased, thus indirectly increasing the risk of AKI.

HEMOGLOBIN:

Anemia prior to surgery injures kidneys by reducing the renal oxygen delivery(82). Lowest hematocrit and oxygen delivery are independent AKI predictors(83). There is progressive increase in the incidence of AKI as the post pump hemoglobin decreased in our study, but this could not attain statistical significance.

50% of patients who had Hb <6gm/dl had AKI, while only 17% patients with Hb > 8gm/dl had AKI.

BLOOD PRODUCTS

As shown by various studies blood transfusion during cardiac surgery is associated with increased mortality (84,85), stroke, low cardiac output syndrome, infective complications and renal failure(86,87).

We infer from our study:

5 of 40 (12.5%) patients receiving one unit of packed cells developed AKI.

8 of 24 (33.3%) patients receiving two units of packed cells developed AKI.

6 of 14 (42.8%) patients receiving more than 3 units of packed cells developed AKI.

On the contrary 10 of 48 (20.8%) patients who did not receive any blood developed AKI.

Incidence of AKI increased as the number of blood units transfused increases.

REEXPLORATION

Taking a patient for reexploration puts him at risk of anesthetic drugs, infection, risk of going on bypass again and its complications. These all can collectively lead to AKI, which may be transient.

In our study only one patient was reexplored for bleeding.

HOSPITAL DAYS:

Increased morbidity due to AKI definitely means increased hospital stay for the patient. In our study on an average the patients were discharged on day 6 post surgery.

MORTALITY

We did not have any mortality in our study. Studies have shown AKI to be independently associated with early mortality(6,71,72).

PREDICTION OF AKI:

Having discussed that AKI is a significant cause of morbidity in the postoperative period in CABG patients, it is important to recognise the risk prior to the procedure. Subsequently,

different clinical scoring systems have been proposed(88). Chertow and colleagues(69) were among the first to developed a risk index to predict postoperative need for dialysis. However, all these proposed clinical scores had limitations including AKI etiology, duration of creatinine or GFR elevation, and recovery of renal dysfunction not being not investigated(69,89,90).

WHAT ABOUT BIOMARKERS FOR PREDICTING AKI:

Urea and creatinine are conventionally used to detect renal function in the post operative period. But these may not be detected early, with abnormal values coming up much later when the injury has occurred(91). The Assessment, Serial Evaluation, and Subsequent Sequelae of Acute Kidney Injury (ASSESS-AKI) study and the Translational Research Investigating Biomarkers Endpoints in Acute Kidney Injury (TRIBE-AKI) study are ongoing prospective cohort studies, evaluating the incremental utility of novel biomarkers—cystatin C, neutrophil gelatinase- associated lipocalin (NGAL), interleukin (IL)-6, IL-18, kidney injury molecule-1 (KIM-1), liver-type fatty acid binding protein (L-FABP), and N-acetyl-_-Dglucosaminidase (NAG)—to refine the diagnosis and prognosis of AKI(92,93).

Thus AKI could be predicted and detected much before it is really causing much damage. Neutrophil gelatinase-associated lipocalin (NGAL) has been investigated extensively and would appear to be one of the most promising early AKI biomarkers(94). It measures tubular stress and is involved in the ischemic renal injury and repair process. It increases dramatically in response to tubular injury. It rises 24 hours prior to creatinine rise.

LIMITATIONS OF THE STUDY

Statistical analysis did not show significant association probably due to small sample size. The number of patients should have been large. This means the study should be for a longer period of time with a larger patient population.

Accurate definition of renal dysfunction: there is no such perfect definition of renal dysfunction. As mentioned various studies use different methods for calculating renal dysfunction. There is no universal definition. The comparison thus becomes difficult.

This is a retrospective study. The prospective design would help in identifying more risk factors in the post operative period like the mean blood pressures in the ICU, urine output in ICU etc.

Ideally creatinine clearance should be used which is a well established indicator of GFR.

The use of nephrotoxic medications and inotropic support were not studied.

CONCLUSION

Incidence of AKI in our study is 23.02%. the incidence of AKI was 4 times more when Mean perfusion pressure was less than 50mmHg. The incidence was also higher in patients more than 60 years of age.

As the number of units of blood transfused increased the incidence of AKI also rises.

Occurance of Acute kidney injury in patients undergoing Coronay Artery Bypass Grafting is a serious complication. It leads to longer hospital stays and thus increases the cost of treatment. Thus identifying them before irreversible injury has occurred is of paramount importance, thus improving patient prognosis. This would demand effort from clinicians and researchers for developing newer strategies and implementing the same.

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APPENDIX

	age	sex	Wt	bsa	DM	ht	lvd	p crt	p gfr	tpt	IS	BL	RE	use	rap	mpp	PHb	Pla	pHb
1	55	2	65	1.82	1	2	2	1.13	53.13	65	34	3	2	2	2	57	6.8	4.6	8.4
2	55	1	89	2.44	1	1	2	1.14	70.88	144	77	0	2	2	2	54	8.4	2.3	11.5
3	44	1	67	1.86	2	2	2	1.18	71.82	41	29	0	2	2	2	52	8.4	1.9	11.8
4	53	2	51	1.54	1	2	2	0.99	63.26	93	53	2	2	2	2	45	6.8	5.5	10.5
5	68	1	75	2.05	2	2	2	1.32	57.33	70	38	2	1	2	2	48	8.1	4.5	10.9
6	55	1	77	2.11	2	1	2	1.2	66.81	44	30	0	2	2	1	49	9.6	4.2	11.5
7	63	1	55	1.62	1	1	2	1.05	75.82	72	39	0	2	2	1	55	9	3.3	13.3
8	61	1	65	1.82	2	2	1	1.15	68.71	78	43	1	2	2	2	44	7.4	4.2	11.5
9	54	1	72	1.97	2	2	2	1.3	61.14	98	55	0	2	2	1	52	9	4.4	11.5
10	56	1	64	1.8	1	1	2	1.42	54.81	54	26	1	2	2	1	50	5.9	2.6	9.9
11	61	1	73	2	2	1	2	1.2	65.42	70	38	0	2	2	2	61	8.7	2.1	11.5
12	54	1	64	1.8	2	2	2	1.18	68.37	45	27	0	2	2	2	56	9	3	13
13	59	1	54	1.6	2	2	2	1.26	62.26	66	29	0	2	2	2	57	7.8	2.9	9.5
14	55	2	68	1.88	1	1	2	1.39	41.84	97	47	3	2	2	2	47	7.8	4	11.2
15	54	2	71	1.94	2	2	2	1.03	1.35	83	43	0	2	2	1	52	6.8	4.8	11.2
16	62	1	64	1.8	2	1	2	1.36	56.44	73	27	0	2	2	2	46	9.2	3.3	12.6
17	54	1	56	1.62	2	1	1	1.1	74.14	107	32	1	2	2	2	56	8.5	2.2	13.6
18	64	1	58	1.68	2	2	2	1.19	65.41	75	44	0	2	2	1	57	9.2	4.7	13.6
19	59	1	56	1.64	1	2	1	1.2	65.87	96	55	1	2	2	2	73	7.8	2.3	11.6
20	63	1	62	1.76	1	1	1	1.35	56.73	92	48	1	2	2	2	56	7.8	2	14.3
21	54	1	70	1.92	1	2	2	1.4	56.13	65	38	0	2	2	1	52	8.5	4.7	11.9
22	50	1	85	2.19	2	1	2	0.93	91.41	64	38	0	2	2	2	58	9.9	3.4	15
23	58	1	62	1.76	2	1	2	1.13	70.84	95	46	1	2	2	1	52	9.2	5.3	12.9
24	60	1	80	2.19	1	1	2	1.52	49.97	82	47	0	2	2	2	61	9.9	3.6	13.6
25	70	1	54	1.6	1	1	1	1.32	56.99	75	38	4	2	2	2	46	7.5	2.7	10.2
26	48	1	65	1.82	1	1	2	1.32	61.53	72	50	1	2	2	1	56	7.8	3.4	12.9
27	53	1	71	1.94	2	1	2	1.19	67.97	94	46	0	2	2	1	55	8.8	2.8	12.2
28	53	1	76	2.05	1	1	1	1.44	54.54	101	57	0	2	2	1	50	7.5	4.3	13.9
29	53	1	60	1.72	1	1	2	0.83	99.98	121	58	0	2	2	1	59	10.2	4	15
30	68	2	55	1.62	1	1	2	1.15	49.87	114	63	5	2	2	2	65	6.8	1.8	9.9
31	67	1	73	2	1	2	1	1.42	52.85	80	48	1	2	2	2	52	8.8	2.1	12.2
32	59	1	65	1.82	1	1	2	1.2	65.87	73	44	1	2	2	1	54	8.8	5.4	13.6
33	53	1	55	1.62	2	2	2	1.23	65.42	64	26	0	2	2	1	48	9.2	4.6	13.2
34	67	2	45	1.42	1	1	2	1.06	54.96	84	47	1	2	2	2	53	6.1	2.1	9.9
35	65	1	73	2.02	2	2	2	1.29	59.41	59	34	0	2	2	2	46	9.2	2.4	15.6
36	56	1	79	2.16	2	2	2	1.26	62.92	77	48	0	2	2	2	49	10.2	1.8	15.1
37	49	1	61	1.74	1	1	2	1.14	72.57	68	48	0	2	2	2	54	8.5	4.4	13.9
38	68	2	61	1.74	2	1	2	0.94	62.94	64	31	0	2	2	2	56	8.5	2.1	13.9
39	50	1	47	1.46	2	1	1	1.33	60.49	68	40	0	2	2	2	45	7.8	5.8	16.1

40	51	1	68	1.88	2	1	2	1.06	78.28	102	56	0	2	2	1	55	9	3.8	12.7
41	58	1	55	1.62	1	2	1	1.22	64.85	61	37	1	2	2	2	51	8.4	3	13.6
42	62	1	65	1.82	2	1	2	1.2	63.26	121	58	5	2	2	2	54	7.8	2.4	10.9
43	62	1	64	1.8	2	2	2	0.84	98.41	87	47	2	2	2	2	48	7.4	3.6	11.6
44	50	1	64	1.8	1	1	2	1.01	83.11	105	45	0	2	2	2	51	8.4	1.9	12.7
45	55	1	64	1.8	2	2	2	1.35	58.32	53	30	1	2	2	1	56	8.7	4.3	13.3
46	59	2	55	1.62	1	1	1	1.25	46.62	99	48	3	2	2	2	55	6.8	2.4	9.6
47	73	1	66	1.84	1	1	1	0.86	92.65	66	37	0	2	2	2	52	8.7	3.9	12.7
48	65	1	62	1.76	1	1	1	1.34	56.86	103	53	3	2	2	2	52	7.4	4.5	9.9
49	62	1	59	1.7	2	1	2	1.06	75.24	120	63	0	2	2	1	50	8.1	3.1	13.6
50	69	2	65	1.82	1	1	2	0.86	69.54	110	55	3	2	2	2	53	6.5	2.7	11.5
51	53	2	45	1.42	2	2	2	0.9	69.61	78	36	0	2	2	2	52	7.8	3	10.9
52	47	1	82	2.24	2	2	2	1.42	56.8	34	22	0	2	2	1	50	8.1	3.4	13.6
53	70	1	51	1.54	2	2	2	1.3	58.01	120	45	2	2	2	2	41	6.8	6.1	11.8
54	55	1	60	1.72	2	2	2	1.26	63.15	83	41	1	2	2	1	50	7.4	5.4	11.8
55	52	2	60	1.72	2	1	2	0.88	71.72	97	50	2	2	2	1	44	7.1	4.2	12.7
56	56	2	48	1.48	1	1	2	1.12	53.49	116	66	3	2	2	1	56	6.8	4.2	10.5
57	53	2	65	1.82	1	1	1	1.02	60.25	84	47	1	2	2	2	54	6.8	5.1	11.5
58	61	1	62	1.76	1	2	2	1.76	62.41	136	69	3	2	2	1	64	6.8	2.1	11.5
59	59	1	63	1.78	1	2	2	0.89	92.99	108	58	0	2	2	2	52	8.1	3.8	11.2
60	43	1	54	1.6	1	2	2	1.25	67	82	48	2	2	2	2	49	9.9	2.4	15.2
61	66	2	67	1.86	1	1	1	0.93	64.11	97	51	1	2	2	2	56	10.2	1.8	11.2
62	63	1	66	1.84	1	1	2	1.19	65.62	94	51	0	2	2	2	52	8.4	2.2	13
63	56	1	86	2.35	1	1	2	1.06	76.81	65	36	0	2	2	2	53	8.4	3.7	13.3
64	69	1	85	2.23	1	1	2	1.19	64.42	112	47	1	2	2	2	45	8.1	4.8	12.1
65	60	1	66	1.84	1	1	2	1.21	65.02	109	61	0	2	2	1	56	8.1	3.6	11.5
66	64	2	50	1.52	2	2	1	1.07	54.87	167	52	3	2	2	2	59	6.5	2.2	9.6
67	49	1	62	1.76	1	1	2	0.89	96.56	133	67	2	2	2	2	52	8.7	3	10.5
68	65	1	61	1.74	2	1	1	1.23	62.77	58	33	1	2	2	2	46	7.4	1.8	12.1
69	57	1	68	1.88	1	2	1	0.86	97.42	91	52	0	2	2	2	51	7.4	2.4	13
70	60	1	81	2.22	1	2	1	1.33	58.29	67	36	0	2	2	2	56	8.7	3.3	12.7
71	65	1	58	1.65	1	1	1	1.12	69.96	60	25	1	2	2	2	51	7.8	3.5	12.4
72	54	1	63	1.78	1	1	2	1.26	63.39	100	58	0	2	2	2	51	8.1	3	13.6
73	48	2	44	1.4	1	2	2	1.06	58.81	77	44	4	2	2	2	43	7.1	3.2	9.6
74	63	2	64	1.8	1	1	2	0.85	71.8	126	61	2	2	2	2	53	10.5	2.9	12.1
75	62	2	55	1.62	2	1	2	1.15	50.82	138	55	7	2	2	2	45	5.6	4.5	12.7
76	48	1	84	2.3	1	1	2	1.13	73.62	93	58	1	2	2	2	43	7.4	2.3	13.3
77	64	1	55	1.62	2	2	2	1.36	56.07	108	60	3	2	2	2	52	6.5	2.7	13.3
78	57	1	49	1.5	2	1	2	1.12	71.82	121	55	1	2	2	1	54	7.4	3.2	12.4
79	62	1	76	2.02	1	1	2	1.15	68.49	99	54	2	1	2	2	50	7.4	2.1	10.5
80	60	1	69	1.9	1	1	2	0.74	99.67	72	25	0	2	1	2	40	8.4	2.5	12.4
81	66	1	65	1.82	1	1	1	1.23	62.57	59	39	3	2	2	2	46	7.4	4.6	11.5
82	57	1	71	1.92	2	2	1	1.07	75.71	141	72	0	2	2	2	61	9.3	2.8	11.8

83	53	1	54	1.6	2	1	2	0.97	86.04	83	42	0	2	2	2	47	8.1	1.7	13
84	55	1	65	1.82	1	1	2	1.03	79.69	102	52	0	2	2	1	50	8.4	2.6	10.7
85	56	1	68	1.88	1	1	2	1.22	65.31	44	26	1	2	2	2	48	8.4	2.7	12.4
86	51	1	61	1.74	1	1	1	1.28	62.97	112	57	2	2	2	2	62	8.1	3.1	13.3
87	65	2	58	1.68	1	2	2	0.96	61.99	72	47	1	2	2	2	54	8.1	5.4	13
88	69	1	52	1.56	2	1	2	1.12	69.09	70	37	2	2	2	2	56	7.1	2.4	10.5
89	64	1	43	1.38	2	2	2	1.1	71.63	113	44	2	2	2	2	57	7.8	1.6	10.2
90	50	1	64	1.8	1	2	2	1.12		125	57	1	2	2	1	56	8.1	3.6	14.8
91	50	1	64	1.8	2	1	2	1.1	75.31	86	48	1	2	2	1	45	6.8	5.4	11.2
92	61	1	64	1.8	1	2	1	1.49	50.96	77	41	2	2	2	2	51	7.1	2	10.9
93	58	1	55	1.62	1	1	2	1.24	63.64	113	60	1	2	2	1	48	7.8	3.8	11.2
94	56	1	55	1.69	2	2	2	1.19	67.21	105	49	2	2	2	2	53	6.8	2.3	13
95	58	1	70	1.92	2	2	1	1.34	58.19	72	42	2	2	2	2	55	7.1	3.3	13.3
96	58	1	66	1.84	1	1	2	1.42	54.42	121	62	2	2	2	2	56	6.5	1.6	9.6
97	60	1	65	1.82	1	1	1	1.43	53.62	87	46	2	2	2	2	45	7.1	3	10.5
98	59	1	65	1.82	2	2	1	1.17	67.82	82	48	1	2	2	1	55	8.7	3.1	11.2
99	62	1	60	1.72	1	1	2	0.99	81.41	142	59	0	2	2	1	58	9.6	4.6	13
100	48	1	60	1.72	2	2	2	0.97	87.3	82	53	0	2	2	1	54	8.7	3.1	12.4
101	47	1	62	1.76	2	2	1	1	85.13	117	65	0	2	2	1	61	8.4	2.8	13
102	70	1	54	1.6	2	1	1	1.26	60.14	115	56	2	2	2	2	59	6.5	4.1	12.4
103	58	1	70	1.92	2	2	2	0.93	88.7	110	52	1	2	2	2	57	8.1	4	12.1
104	55	1	41	1.33	2	1	1	1.05	77.94	163	78	3	2	2	2	56	7.1	3.4	9.6
105	59	1	79	2.16	1	2	1	1.09	73.59	61	33	0	2	2	2	47	9	5.5	14
106	55	1	78	2.13	2	1	1	1.1	73.87	102	55	0	2	2	2	51	8.7	5.4	11.8
107	59	1	62	1.76	1	2	1	1.32	59	46	17	0	2	2	2	54	9	3.1	15.2
108	58	2	52	1.56	1	1	2	1.14	52.03	107	52	2	2	2	2	57	7.4	3.9	9.9
109	64	2	65	1.82	2	1	1	1.06	55.47	63	39	2	2	2	2	53	6.2	3.3	10.5
110	59	1	56	1.64	2	1	1	1.06	76	93	39	0	2	2	2	49	8.1	2.1	13
111	67	1	67	1.86	2	2	1	0.89	90.67	150	54	3	2	2	2	56	6.8	6.3	12.1
112	55	1	61	1.74	2	1	2	1.03	79.69	109	66	1	2	2	2	60	7.1	2.8	9.3
113	66	1	54	1.6	2	2	2	1.39	54.39	64	39	3	2	2	2	58	6.8	3.5	8.4
114	62	1	56	1.64	2	1	1	1.08	73.64	91	43	2	2	2	2	49	7.1	4.2	9.9
115	65	1	47	1.46	2	1	2	0.97	82.56	116	56	1	2	2	2	46	7.8	4.5	14
116	56	2	48	1.46	2	2	1	0.96	63.9	58	25	0	2	2	2	44	6.8	4.8	12.4
117	52	1	55	1.62	1	1	2	1.08	76.31	117	63	2	2	2	2	52	6.5	3.2	10.5
118	56	1	69	1.96	1	1	1	1.17	68.54	66	42	3	2	2	2	47	5.9	3.1	10.9
119	68	1	76	2.08	2	1	2	1.08	72.07	136	64	2	2	2	2	57	8.7	3	12.4
120	50	1	58	1.68	2	2	1	1.24	65.59	113	61	2	2	2	2	42	9	4.1	14
121	59	1	69	1.9	2	1	2	0.99	82.24	93	50	1	2	2	2	45	8.4	3.7	14
122	58	1	65	1.82	2	1	2	1.13	70.84	98	52	0	2	2	1	57	9.9	1.7	14.3
123	61	1	64	1.8	2	1	1	1.18	66.7	94	55	1	2	2	2	59	7.8	2.2	12.1
124	55	1	59	1.7	1	1	2	0.8	99.98	93	49	1	2	2	2	61	9.3	4.6	14.3
125	66	2	67	1.86	2	2	2	0.78	78.54	69	45	4	2	2	2	54	7.1	4.8	10.5

126	42	1	61	1.74	1	1	2	1.15	74.12	94	50	1	2	2	2	58	8.1	5.3	12.7
127	60	1	54	1.6	1	2	2	1.07	74.93	88	50	0	2	2	2	58	8.7	1.4	12.4
128	58	2	49	1.5	2	1	2	1.07	55.98	104	60	2	2	2	2	56	7.1	3.8	13
129	66	1		1.82	1	1	2	1.1	71.18	77	37	3	2	2	2	51	7.4	4.1	9.9
130	60	1	71	1.94	1	1	2	1.11	71.82	59	33	1	2	2	2	57	7.1	2.3	14.3
131	59	2	38	1.27	1	1	2	0.83		121	44	2	2	2	2	57	7.4	3.5	10.9
132	58	1	55	1.62	1	2	1	0.81	99.03	104	53	1	2	2	2	55	8.4	4.2	12.7
133	63	1	56	1.64	1	1	2	1.22	63.77	65	39	2	2	2	2	60	6.8	2.7	9.6
134	56	1	63	1.78	1	1	2	1.15	69.92	130	79	2	2	2	1	54	6.2	2.3	11.2
135	63	1	66	1.84	1	1	1	0.76	99.1	48	21	0	2	2	2	49	10.2	2.7	15.5
136	57	1	60	1.72	1	1	2	1.21	62.13	100	56	2	2	2	2	58	7.8	3.3	11.8
137	63	1	63	1.78	1	1	1	1.12	70.38	59	34	1	2	2	2	52	8.4	3.2	11.5
138	53	1	66	1.84	2	1	2	1.05	78.53	87	49	1	2	2	2	49	8.7	3.7	12.7
139	61	1	84	2.3	1	1	1	0.99	81.68	108	55	0	2	2	1	59	9.3	4.4	12.2
140	60	1	68	1.68	1	1	2	1.17	72.57	31	19	1	2	2	2	53	7.1	4.5	11.8
141	46	1	58	1.68	1	1	1	1.35	60.47	104	52	2	2	2	2	49	9.6	4.5	30.3
142	54	1	40	1.44	1	2	1	1.13	71.88	73	35	2	2	2	2	40	6.8	3.2	11.5
143	67	1	70	1.92	1	1	2	1.27	60.12	95	62	3	2	2	2	53	7.4	3.5	10.9
144	48	1	76	2.08	2	2	2	0.91	94.51	102	54	0	2	2	2	49	8.4	1.8	12.4
145	66	1	82	2.24	1	1	2	1.12	69.72	104	56	3	2	2	2	50	7.8	4	13
146	45	1	61	1.71	2	1	2	1.1	76.94	107	59	0	2	2	2	49	9.3	3.5	14.3
147	53	1	65	1.82	1	1	2	1.24	64.82	65	35	3	2	2	2	50	6.5	3.5	12.1
148	58	1	75	2.05	1	1	2	1.21	65.46	106	51	1	2	2	1	57	8.1	3.9	13.6
149	63	1	66	1.84	1	1	1	1.08	72.71	90	42	1	2	2	2	51	7.2	2.1	1.1
150	68	1	68	1.8	1	1	2	1.34	56.34	88	52	0	2	2	2	61	7.4	2.8	14.9
151	68	1	90	1.92	2	1	1	1.29	58.87	82	47	0	2	2	2	58	6.8	1.3	12.4
152	58	1	66	1.84	1	1	1	1.07	54.79	132	56	1	2	2	2	62	9	6.8	14
153	65	1	62	1.62	1	2	1	1.21	63.97	97	56	2	2	2	2	62	5.6	1.5	12.4
154	33	1	61	1.44	1	1	2	0.8	99.48	103	54	1	2	2	2	64	7.1	2.2	11.5
155	73	1	62	1.76	1	1	2	1.14	66.93	66	38	3	2	2	2	56	9	3.1	14.3
156	60	2	55	1.62	2	1	2	0.92	66.18	98	54	2	2	2	2	66	6.2	3.8	12.1
157	62	1	55	1.68	1	1	2	1.1	72.09	98	42	0	2	2	2	62	8.4	3.6	14
158	49	1	59	1.7	2	2	1	1.34	60.22	56	23	0	2	2	2	44	8.7	3.3	16.1
159	52	1	70	1.92	1	1	1	1.25	64.47	109	62	1	2	2	2	48	7.8	3.9	12.8
160	53	1	74	2.02	1	1	2	0.84	99.59	145	83	0	2	2	2	60	8.4	1.4	13.3
161	57	1	76	2.08	2	1	1	1.12	71.82	84	53	1	2	2	2	54	7.1	3.2	12.7
162	38	1	54	1.6	1	1	1	0.92	97.86	104	64	1	2	2	2	63	6.2	1.8	13
163	58	1	49	1.5	2	2	2	1.01	80.64	141	62	1	2	2	1	61	8.7	2.5	12.4
164	58	1	48	1.4	2	2	2	1.04	80.74	142	53	1	2	2	1	62	8.8	2.4	12.4